GEORGIA INSTITUTE OF TECHNOLOGY
INSTITUTIONAL REVIEW BOARDS

Policies & Procedures Manual

Federalwide Assurance Approved by
Office for Human Research Protections
FWA00001731

Central Institutional Review Board
IRB00000548

September 2026
Georgia Institute of Technology
Institutional Review Board

Revisions and Updates

September 2026:

- VI: Updated the Eligibility Exceptions for Graduate and Undergraduate Students as Principal Investigators to include additional information

June 2025

- Appendix 11: Updated GT Stamps Services information to reflect current GT Stamps Policies.

July 2024

- III: Updated broken links to external sites to reference appropriate Ga. Codes.
- IX: Updated broken links, fixed typos, removed pronouns, and revised information to accurately reflect the requirements for Exempt submissions.
- X: Updated broken links.
- XII: Updated list of contacts in the request to use student data SOP in section C.
- XXVII: Updated information regarding the GT office who handles conflicts of interest.
- XXVIII: Updated contact information for the IRB in example addendum.
- Appendix 9: Updated link to current NIH policy.
- Appendix 11: Updated criteria for obtaining blood to be in line with the Expedited categories and updated CDC links.
- Appendix 21: Added missing information from guidance document and fixed formatting of table of contents.
- Appendix 26: Updated EU GDPR documents to current versions which include UK as well.

April 2024

- VII: Revised the information regarding what documents are needed when submitting a study for Exempt Review.

February 2024

- XI: Removed specific reference to child advocate that sits on the GT Central IRB and rephrased wording within the first paragraph.

January 2024

- V: Removed reference to DOD and FWA requirement for CITI training.
- VII: Added new FLEX 2 and 3 categories of Exempt research, where the study must meet very specific criteria to be eligible for this type of research.
- IX: Revised the section regarding additional requirements from the DoD as the information was inaccurate.
- XXXIII: Removed references to positions that no longer exist.

- XXXIV: Added this section to discuss how the Pre-2018 Common Rule still applies to research that was approved or determined to be Exempt prior to January 21, 2019, when the 2018 Common Rule became effective.

September 2023

- IV: Changed CROO to AVP-RIA.

June 2023

- I: Fixed grammar and removed reference to multiple GT IRB committees.
- II: Removed reference to VPR and added reference to IO.
- III: Removed pronouns.
- IV: Changed EVPRDO to CROO and fixed old or broken links.
- V: Changed EVPRDO to IO, removed pronouns, and changed Research Associate to ORIA staff member.
- VI: Changed EVPRDO to IO and removed pronouns.
- VII: Changed reference to Research Associate to ORIA staff member.
- VIII: Fixed links to the Common Rule.
- IX: Fixed link to another section within the document and removed pronouns.
- X: Updated the information regarding what office the Conflict of Interest team falls under and removed pronouns.
- XI: Removed pronouns.
- XII: Removed pronouns.
- XV: Fixed broken link to NIH website.
- XVII: Fixed typo.
- XIX: Fixed formatting within the section.
- XX: Added a new section specifically regarding tribal research.
- XIX – XXIII: All sections were re-numbered by increasing by one (e.g., XX to XXI).
- XXI: Fixed formatting within the section.
- XXII: Fixed broken link to ORIA webpage and removed pronouns.
- XXIII: Fixed link to GTRC webpage, removed pronouns and removed reference to VPRDO.
- XXVI: Changed reference regarding where visiting scholar agreements are sent from Legal Affairs to the associated academic department and removed pronouns.
- XXVII: Changed GTRC to GT in reference to where the COI team is located and removed pronouns.
- XXX: Removed phone numbers for specific ORIA staff, removed broken links to external webpages, removed pronouns, and fixed formatting.
- XXXI: Removed pronouns.
- XXXII: Fixed formatting within the section.
- XXXIII: Removed reference to VPRDO.
- Appendix Table of Contents: Fixed links to specific appendices.

- Appendix 3: Fixed and removed broken links to NIH.
- Appendix 4: Fixed broken links to GT Library websites.
- Appendix 6: Updated compensation information in the brochures to participants.
- Appendix 12: Removed sample and re-wrote appendix to be consistent with the information provided by the Office of Sponsored Programs.
- Appendix 15: Revised the information regarding scientific review so that it is consistent with DoD policy.
- Appendix 16: Revised the information regarding when scientific review is needed.
- Appendix 18: Revised the section to reflect the final guidance document from the FDA.
- Appendix 21: Revised the section to reflect the final guidance document from the FDA.
- Appendix 23: Revised to state that only non-exempt studies need a certificate of translation and removed the reference to the cost.

December 2022

- IX: Re-arranged the information under the sub-header C, Protocol Sign-offs, to fully explain the purpose of departmental sign-off and renumbered the information under this sub-header.
- XX: Clarified that the Office of Research Integrity Assurance can make IDE Exempt determinations.

November 2022

- XII: Updated the name of the IRB contact in the Request to Use Student Data document.
- XXX: Removed the maximum number of continuing reviews that can be submitted for each study and renumbered the remaining parts of this section to account for the removal of section XXX.B.4. Maximum Number of Continuing Reviews.
- Appendix 1: Updated both Template 1 and 2 to remove the contact information for specific individuals and left the general email address for the IRB.
- Appendix 7: Updated the template to remove the contact information for specific individuals and left the general email address for the IRB.

July 2022

- I: Updated to reflect the current Georgia Institute of Technology Strategic Plan
- III: Updated information regarding Phase II and Phase II Cancer Clinical Trials subsection to reflect current Georgia code regarding this topic.
- IV; Fixed typos and updated information to reflect the current reporting structure for the Office of Research Integrity Assurance.
- V – IX: fixed multiple typos.

- X: Fixed typos, updated language regarding audio and video recordings to be more inclusive to digital technology, and fixed broken links.
- XI: Fixed broken links.
- XII: Fixed typos and updated language regarding audio and video recordings to be more inclusive to digital technology.
- XV: Fixed broken links.
- XVI: Fixed broken links and removed out-of-date information regarding continuing reviews.
- XVII: Fixed typos.
- XXI: Fixed broken links and typos.
- XXIX: Fixed broken links and updated the phone numbers listed to the current GT IRB contact phone numbers.
- XXX: Fixed broken links.
- Appendix 3: Updated information to reflect current FDA guidance regarding FDA issued Certificates of Confidentiality.
- Appendix 15: Fixed typos.
- Glossary: Fixed broken links and typos.

February 2022

- Appendix Table of Contents: Updated title of Appendix 1.
- Appendix 1: Updated title to be more inclusive and updated the Confidentiality section in consent document to reflect current language found in the current consent template.
- Appendix 2: Updated the Confidentiality section in consent document to reflect current language found in the current consent template.

July 2021

- The Joint GSU-GT Center for Advanced Brain Imaging (CABI) IRB has been dissolved. Therefore, any reference to the Joint GSU-GT CABI IRB and any reference to Georgia Tech having multiple IRB's has been removed from the following sections.
    - Cover page, I, IV, V, VIII, IX, XI, XIV, XV, XIX, and Appendix 15 (formerly Appendix 16).
- The Institutional Official (IO) for Georgia Tech has been changed from the Vice President of Research (VPR) to the Vice President of Research Development and Operations (VPRDO). This change has been made in the following sections:
    - IV, V, XXII, and XXXII
- IX: Information regarding DoD required training has been updated and the required information regarding Georgia Tech's accounting procedures involving compensation has been updated to the current information.
- XII: A reference to a specific online survey platform has been revised and generalized.

- XIV: The required information regarding Georgia Tech's accounting procedures involving compensation has been updated to the current information.
- XV: Fixed a typo
- XXIX: A reference to the Center for Advanced Brain Imaging was revised to reflect the proper name of the facility.
- Appendix Table of Contents: Appendices 13 and 28 were removed from the list and all numbers for appendices 14-26 were updated.
- Appendix 4: Fixed a typo
- Appendix 13: This appendix was specific to the Joint GSU-GT CABI IRB, which has been dissolved. Therefore, this appendix was removed.
- Appendix 28: This appendix was specific to Georgia Tech's COVID-19 response in regards to human research practices. This appendix was removed as this is not an IRB policy and the policy currently lives outside this set of policies.
- Appendices 14-27: All of the appendix numbers were revised to reflect the deletion of appendix 13. Therefore, every appendix between 14 and 27 has been lowered by one number.
- Entire document: All references to appendices 14 through 27 have been updated to reflect the new numbering.

March 2021

- VII: Removed 'certified translations' from the list of examples of the type of documents that are required for Exempt review.
- IX: Removed 'certified translations' from the list of examples of the type of documents that are required for Exempt review.
- XIX: Added a note that certified translations may not be required for Exempt studies.
- Appendix 24: Added a note that certified translations may not be required for Exempt studies.
- Appendix 28: Updated the COVID-19 documents to provide information regarding the contact tracing requirement, to revise information about the availability of vaccines, to update information regarding specific populations that are and are not allowed to be enrolled in research at this time, and to fix several typos.

July 2020

- Appendix 28: Updated policy to fix typos.

June 2020

- Updated all references to appendices after Appendix 16 to update numbering.
- XXIII: Revised to reflect changes to Conflict of Interests policy.
- Appendices Table of Content: Updated to reflect removal of Appendix 17 and addition of Appendix 28.
- Appendix 11: Revised to allow and provide procedures for in-lab blood collection.

- Appendix 16: Updated to reflect changes to DON training requirements.
- Appendix 17: Removed from document as DON no longer requires their own specific training.
- Appendix 28: Added to discuss restart of non-essential in-person human subjects research during the COVID-19 pandemic.

April 2020

- Appendix 16: Revised to reflect revised DoD policy in regards to human subjects research.

March 2020

- Revised Table of Contents link in the footer of the document to better reflect the purpose of the link.
- Updated all GT specific emails and websites to reflect new domain.
- VII: Updated policy to reflect new procedures for submitting Exempt Review submissions to the IRB.
- IX: Updated policy to include information regarding HIPS, GCP, and Social and Behavioral Good Clinical Practice CITI training.
- IX: Updated policy to remove information regarding NIH human subjects training.
- IX: Updated policy to remove duplication of information.
- IX: Updated policy to reflect new procedures for submitting Exempt Review submissions to the IRB.
- XII: Updated policy to include the Registrar's Office new policy concerning all research involving FERPA protected data.
- Appendix 13: Revised policy to reflect current process for obtaining CABI IRB Full Board approval.
- Appendix 16: Revised to reflect revised DoD policy in regards to human subjects research.
- Appendix 17: Updated information to provide a more accurate guide on how to complete the DON CITI modules.

October 2019

- Fixed and updated wording in Appendix 1 and 2.
- Glossary: Updated definition of "Clinical Investigation" and changed term to "Clinical Study."
- Glossary: Updated definition of "Clinical Trial."
- Glossary: Added definition of "Applicable Clinical Trial."
- Glossary: Added definition of "Applicable Device Clinical Trial."
- Glossary: Added definition of "Applicable Drug Clinical Trial."
- Glossary: Added definition of "NIH Clinical Trial."

September 2019

- Fixed and updated links in the Research in International Settings section.

August 2019

- Fixed and updated links on Appendices Table of Contents.

May 2019

- X: Updated information regarding Waiver of Informed Consent.

March 2019

- VI: Updated description of postdoctoral fellows.
- VII: Added information regarding Limited IRB Review.
- VIII: Added policy describing when IRB review and approval is needed for de-identified data and de-identified specimen research.
- XV: Updated information regarding types of review required.
- Re-formatted all sections and appendices.

January 2019:

- Updated all references and links to the 2018 Common Rule (§45CFR46).
- VII: Updated the Exempt Categories and specific information regarding Subparts B, C, and D.
- VIII: Updated the definitions to Research and Human Subjects.
- IX: Added information regarding Limited IRB Review.
- X: Added information about Key Concepts and updated the Waiver of Consent and Waiver of Documentation of Consent criteria.
- XI: Updated information regarding Exempt in regards to Subparts B, C, and D.
- XV: Updated information regarding Waiver of Consent criteria, when consent is required, and types of review required.
- XXVI: Updated section to reflect new regulations concerning continuing review.
- XXX: Updated section to reflect new regulations concerning continuing review.
- Appendix 2: Re-formatted text.
- Appendix 3: Updated appendix to reflect the 2017 NIH COC policy.
- Appendix 8: Updated the table to reflect the 2018 Common Rule regulations.
- Appendix 13: Updated GSU and GT contacts listed appendix.
- Glossary: Updated the definitions.

November 2018:

- IV. Updated section to remove reference to the classified research IRB, as this IRB no longer exists at Georgia Tech.
- XXIII. Updated title and added section to include MOU in place with the University of Georgia.

October 2018:

- III. Updated links to current State of Georgia laws.
- XV. Updated links to current U.S. Senate webpage.
- XVI. Updated links to current NIH COC webpage.
- XX. Updated links to current FDA webpages.

- XXII. Updated link to current GT Grants webpage.
- XXX. Updated links to current GT IRB webpage.
- Re-formatted all sections and appendices so that they properly display in table of contents.
- Roman numeral for all sections between and including Section XI. (Research Involving Georgia Tech Students at Participants) and section XXXII. (Reporting Violations of the Georgia Institute of Technology Institutional Review Board Policies and Procedures) were increased by one Roman numeral.
- Table of contents updated.
- Appendix list updated.
- Appendix 28: Added EU GDPR Policy and links
- X A. 5. Updated website link to https://security.gatech.edu/information-security-procedures-and-standards.
- X B. 1. Updated website link to http://researchintegrity.gatech.edu/irb/hsr/irb-informed-consent.
- XI A. 2. Updated website link to http://researchintegrity.gatech.edu/irb/submitting-protocol/forms.
- XXI H. Updated website link to http://researchintegrity.gatech.edu/irb-required-training.
- XXII A. 2. Updated website link to http://www.grants.gatech.edu/grants-and-contracts-accounting-policies-and-procedures.
- XXV. A. Updated document title to BOR Practice Manual.
- XXV. A. Updated website link to https://www.usg.edu/hr/manual.
- XXV A. Updated website link to http://www.policylibrary.gatech.edu/mandatory-reporting-child-abuse-policy.
- Appendix 1: Removed email address for Barbara Henry.
- Appendix 2: Removed email address for Barbara Henry.
- Appendix 4: Updated website link to https://security.gatech.edu/information-security-procedures-and-standards.
- Appendix 7: Removed email address for Barbara Henry.
- Appendix 13: Removed Barbara Henry from list of contacts.
- Appendix 13: Changed role for Kelly Winn to Director.

January 2018:

- Final Rule Updates
- Revise definition of “research” to include new carve-outs.
- Revise definition of “human subject.”
- Revise existing exemptions.
- Include new exemptions.
- Document process and conditions for limited IRB review for exemptions (d)(2), (d)(3), (d)(7), and (d)(8).

- Revise continuing review policy to account for new carve-outs and to require documentation of rationale if IRB will conduct continuing review when not otherwise required.
- Revise expedited review procedures to include research for which limited IRB review is conducted and to require documentation of rationale if reviewer determines research on the expedited review list is more than minimal risk.
- Revise waiver process to reflect limitation when broad consent ii sought and refused. Determine how refusals of broad consent will be tracked.
- Revise screening and recruitment policy to reflect elimination of requirement for consent (or waiver) for these activities.
- Revise specific consent template to reflect new elements and organization of consent.
- Create new broad consent template (and potentially combined broad/specific consent template where secondary research is contemplated).
- Discuss internally how the changes to informed consent interact with the institution's requirements related to HIPAA authorization in the context of secondary research.
- Update investigator guidelines for informed consent (if applicable) to reflect changes and explain context for use of specific vs. broad consent and how they relate to one another.
- Revise policy on documentation of consent and waiver of documentation to reflect new requirements for when short form may be used and new basis for waiver of documentation.
- Create policy on posting of consent forms for clinical trials to public federal website.
- Create or revise policy on legally authorized representatives to include individuals acceptable for providing consent to a subject's participation in the procedures involved in the research.
- Revise IRB application forms to reflect new definitional carve-outs, exemption categories, and research eligible for expedited review.
- Consider revising the IRB consent waiver application form to seek an investigator certification that broad consent was not previously sought and refused.
- Consider creating separate IRB application form for limited IRB review, targeting the information necessary to meet the required conditions.
- Ensure all current reliance arrangements with external IRBs are documented and that the respective responsibilities of the institution and the external IRB(s) are set forth in the agreement or otherwise in an institutional policy.
- Develop or revise policy on cooperative research to reflect single IRB mandate and NIH Single IRB Policy.
- Develop or revise IRB reliance agreement template(s).

- Assess institutional reliance relationships and determine whether the number can be streamlined by participating in large network arrangements and/or "master" agreements covering multiple protocols.
- Designate a local point person for coordination and tracking of reliance relationships and communication with external IRB(s).
- Identify IT systems to help manage/track reliance relationships.
- Develop local context information sheet and plan for coordination with external IRB(s) re: institutional issues (e.g., ancillary reviews, coordination of consent forms with sponsored research contract provisions).
- Develop information sheet to gather key information about external IRB(s) or institution(s) seeking to rely on the local IRB.
- Train investigators on expectations for working with external IRB(s).
- For institutions that have "checked the box" on their Federalwide Assurance, determine any implications of removal of option to check the box (e.g., under state laws referencing compliance with federal human subject standards).
- Identify existing databases and repositories in which information and materials are stored for possible secondary research purposes.
- Determine whether existing repositories will remain governed by the pre-2018 Common Rule, or whether a voluntary shift to compliance with the 2018 Common Rule will occur.
- Determine which on-going research studies subject to the Common Rule will straddle the general compliance/effective date.
- For each identified study, determine whether to continue to comply with the pre-2018 Common Rule, or elect to comply with the 2018 Common Rule (assuming an IRB documents the institution's determination).
- Develop and implement mandatory training sessions for IRB members, institutional officials, and the research community (investigators, research coordinators, and other research staff) to apprise them of the significant changes in the 2018 Common Rule.
- Consider making a web portal of resources and investigator guidance documents available to researchers, including an investigator-focused compliance checklist, to enlist investigators in relevant preparation steps ahead of the general effective / compliance date.

August 2016:

- Appendix 10: Added NIH's change in definition of *children in clinical research* to guidance regarding the inclusion of children as participants in research involving human subjects
- Various. Removed references to an Umbrella form

January 2016:

- V.E. Added "Visitors at IRB Meetings"

November 2015:
- IX A.3. Updated guidance on expired training

September 2015:
- Appendix 16: Added item 23 "PRINCIPAL INVESTIGATOR ACTIONS," guidance for Principal Investigators regarding process to secure DOD-agency approval when a protocol is subject to the Department of Defense Addendum to Georgia Tech's Federalwide Assurance

April 2015:
- XVI. Added guidance on Repositories, Tissue Banks and Biobanks; Registries and Data Banks; and Databases
- Added Appendix 26, *Sample Repository Submittal Agreement*
- Added Appendix 27, *Sample Repository Sharing Agreement*

March 2015:
- XIII.C. Regarding institutional policy that neither employees nor students may participate as human subjects on a project to which their compensation is charged: clarifies that consultants are also prohibited from such arrangements.
- XII. Sets forth additional consent criteria for proposed disclosure of students' personally identifiable information from education records by an educational agency or institution.

January 2015:
- I. Mission: Update mission statement.
- APPENDIX 16, Additional Requirements for Research Involving Department of Defense. Added link to *"Guidelines for Investigators: Requirements for U.S. Army Medical Research and Materiel Command (USAMRMC) Headquarters."*

December 2014:
- IX.C.3. Adds guidance relating to vehicular transportation of human research subjects by Georgia Tech personnel
- XXVIII.A.4. Clarifies that anticipated adverse events of minimal risk may be reported at time of annual renewal.

October 2014:
- Glossary. NIH issued 'Notice of Revised Definition of *Clinical Trial*.'
- V.3. Revised Conflict of Interest language relating to board members participating in discussion and vote.
- XXIV. Clarified guidance regarding Non-Georgia Tech Personnel (including Visiting Scholars and Minors) Participating in Protocols at Georgia Tech.

January 2014:

- Appendix 6. Rephrased statement about identifiers being replaced with a code.
- XXVI. "Investigator's Responsibilities When Conducting Research Activities Subject To DHHS" was modified to add "Identifying the Point When Continuing Review Is No Longer Necessary."

July 2013:

- Appendix 11. Clarified that blood draws shall be done at Stamps Health Services or Concentra Health Services by professional phlebotomists.

June 2013:

- Glossary: Updated the definition of *Guardian* in accordance with revisions by the Food & Drug Administration
- IV.A. Added the Institutional Review Boards' registration numbers on file with the federal Office for Human Research Protections
- XXII. Added process describing reliance by the Georgia Tech IRB upon the IRB at another institution

May 2013:

- XVII. Clarification of policy regarding conduct of human subjects research in private residences
- Appendix 25: Translation of documents

April 2013:

- Complete review of contents
- Appendix 4: Amended to add new information regarding "Scholarly Materials and Research @ Georgia Tech" (SMARTech), located at https://smartech.gatech.edu/, an institutional repository available to researchers whose funding agency or other organizations do not maintain a data archive or repository that will accept research data.

March 2013:

- Appendix 24: Establishes written procedures for the reliance by another institution on the Georgia Tech IRB
- XXIV. Minor update to guidance regarding Visiting Scholars Participating in Protocols at Georgia Tech

January 2013:

- X.D.2.; IX.B.7.b.; XVIII.D. Adds requirement that consent form and other documents that must be translated from or to English must be accompanied by a certified, professional translation.
- XIX. Updates guidance on Research Subject to the Food & Drug Administration (FDA): Medical Devices or Investigational New Drugs
- XXV. Updates guidance on Investigator's Responsibilities When Conducting Research Activities Subject to DHHS

November 2012:

- Updates title of Compliance Officer to Research Associate
- Updates website links to http://www.researchintegrity.gatech.edu

August 2012:

- VI.D. Adds Circumstances that Render Researcher Ineligible to Hold Role of Principal Investigator, Co-Principal Investigator, or Investigator
- Appendix 19: Sample Investigator Agreement for Clinical Trials
- XIX. Adds guidance about Case Report Forms
- Appendix 20: Adds Nanotechnology Guidance: FDA Draft Guidance on *Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology*, dated June 2011

July 2012:

- XXII.D. Adds Children's Hospital of Atlanta and Georgia Institute of Technology Authorization Agreement

June 2012:

- Changes name of the Office of Research Compliance to the Office of Research Integrity Assurance
- Adds page numbers to the Table of Contents

May 2012:

- XIII.D. Adds Prohibition on Georgia Tech Employees Being Used as Research Subjects as a Condition of Employment

March 2012:

- XIII.B. Corrects guidance on compensation to Georgia Tech employees
- Adds required language to consent documents for clinical studies subject to FDA

January 2012:

- VI. Updates eligibility for the title of Principal Investigator

October 2011:

- Appendix 16. Further clarifies guidance and provides specific requirements by individual DOD agencies Additional Requirements Incorporated by Addendum to Federalwide Assurance for Research Involving Department of Defense
- Appendix 17: Instructions on Accessing CITI Modules Required by Navy
- Appendix 18: Scientific Review Template for DOD Protocols

September 2011:

- IX.A. Training in Human Subject Protection: Only CITI training will be accepted for human subjects training. Completion of PSYC 2020 or 6018 courses will no longer satisfy the training requirement. Students who have taken those courses will need to complete the applicable CITI training modules.

July 2011:

- IX.A. Procedures for Obtaining Institutional Review Board Approval: Updates training requirements by adding CITI module refresher courses every three years.
- XVIII. Research in International Settings: Updates and clarifies requirements, corrects OHRP website address for the International Compilation of Human Subject Research Protections.
- XI. Research Involving Vulnerable Populations: Children, Prisoners, Pregnant Women and Fetuses: The Central IRB is now constituted to review research protocols involving prisoners.
- XXX.F. Guidance on Reporting Incidents (non-compliance) to the Office for Human Research Protections
- IV.D.1. Federalwide Assurance and Administration of Georgia Tech Program of Human Research: Clarifies policy on retention of IRB records, including protocols.

June 2011:

- Updates title of Institutional Official to Vice President for Research

January 2011:

- XV.D. Updates language on genetic studies in accordance with NIH guidance

September 2010:

- XII.A.2. Addresses enrolling Georgia Tech students when a waiver of documentation of consent is approved.

July 2010:

- XXV.6.B. Clarifies when continuing review is required for protocols closed to enrollment.

January 2010:

- XIV.H.1. Addition of guidance regarding payments to nonresident aliens, "Compensation to Nonresident Aliens." Modification of consent templates to disclose resulting requirement for collection of subject addresses and citizenship/visa status.

December 2009:

- Minor corrections to numbering of Appendices.

September 2009:

- XI.A.2. Parental or Guardian Permission and Assent: Added language precluding the use of implied parental permission.
- XXII.C. Consent Harmonization with Shepherd Center: Added the informal agreement between Georgia Tech and Shepherd Center regarding harmonization of consent forms used in a collaborative study.

- Appendix 14: Enrolling Oneself as a Subject in One's Own Study - "Self-Experimentation"
- XVII. Off-Campus Study Locations, including Private Residences, Daycare Facilities, Elementary and Secondary Schools: Clarified when written site permission is required. Added sample school and other site permission letters at Appendix 14.
- XI. Research Involving Vulnerable Populations: Children, Prisoners, Pregnant Women and Fetuses: The Central IRB is now constituted to review research protocols involving prisoners.
- XXX.F. Guidance on Reporting Incidents (non-compliance) to the Office for Human Research Protections
- Appendix 16. Additional Requirements for Research Involving Department of Defense incorporated by Addenda to Federalwide Assurance.

GEORGIA INSTITUTE OF TECHNOLOGY
INSTITUTIONAL REVIEW BOARD POLICIES & PROCEDURES
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Georgia Institute of Technology
Institutional Review Board
POLICIES & PROCEDURES

I. Mission

Reviewed: July 2024

The Georgia Institute of Technology's Institutional Review Board is charged with the responsibility of safeguarding the rights and welfare of human participants in research. The board's missions directly support the institute's strategic plan, with particular emphasis on the strategic goals to "Amplify Impact" and "Champion Innovation."

The university's program of human research participant protection is based on the three primary ethics principles set forth in the Belmont Report, issued in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research:

- Respect for persons,
- Beneficence, and
- Justice.

The Georgia Institute of Technology Institutional Review Board will apply these principles to all human research projects, regardless of sponsorship.

II. Institutional Commitment to the Protection of Human Research Participants

Reviewed: July 2024

Safeguarding the rights and welfare of human participants in research is an institutional policy directed by the President through the Executive Vice President for Research and the Institutional Official. It is their responsibility to exercise appropriate administrative oversight to assure that Georgia Tech's *Policies & Procedures* designed for protecting the rights and welfare of human participants are effectively applied in compliance with the university's Federalwide Assurance.

III. Statutory Basis of Institutional Review Board Authority

Revised: July 2024

The IRB is an administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the Georgia Institute of Technology. The IRB has the authority to approve, require modifications in, or disapprove all research activities that fall within its jurisdiction as specified by both the federal regulations and Georgia Tech policy. Per §45CFR46.112, research that has been reviewed and approved by an IRB may be subject to review and disapproval by officials of the institution. However, those officials may not approve research if it has been disapproved by the IRB.

The Georgia Tech program of protections for human research participants is subject to regulation and inspection, as provided in the regulations cited below.

A. Department of Health and Human Services (DHHS)

DHHS regulations pertaining to rights and welfare of subjects participating in research supported with federal funding are specified in *Title 45 Code of Federal Regulations Part 46*, "Federal Policy for the Protection of Human Subjects" and including *Subparts A, B, C, and D*.

B. Food and Drug Administration (FDA)

FDA regulations pertaining to rights and welfare of subjects participating in research involving drugs, medical devices, and biological products and other products regulated by the FDA are specified in *Title 21 Code of Federal Regulations, Parts 50* Protection of Human Subjects, *56* Institutional Review Boards, *312* Investigational New Drug Application, and *812* Investigational Device Exemptions. See *Appendix 19* for FDA guidance on the responsibilities of researchers conducting work subject to FDA.

C. State of Georgia

1. Prisoner Studies

Medical experiments involving prisoners require prior written approval of the Commissioner of Corrections. Ga. Comp. R. & Regs. 125-4-4-.12.

2. Genetic Research

Genetic information is the unique property of the individual. Its use may be abused if disclosed to unauthorized third parties without consent. Official Code of Georgia Annotated 33-54-1. Definition of "genetic testing." Ga.Code 33-54-2. Informed consent required prior to genetic testing for insurance reasons. Ga.Code 33-54-3. Genetic information may be released only to the individual tested or authorized persons or to a third party with explicit written consent. Ga.Code 33-54-3. Insurers may not use genetic information for nontherapeutic purposes. Ga.Code 33-54-4 (but see Ga.Code 33-54-7). Research facilities may conduct genetic testing and use the information for scientific research purposes if the individual's identity is not disclosed. Ga.Code 33-54-6.

3. Consent Age

The State of Georgia defines minors as those persons under the age of 18 years. Emancipated minors may participate in some studies otherwise unsuitable for children, provided adequate justification. *Note that in its definition of children in clinical research, the National Institutes of Health, effective 2016, states that "…for the purposes of inclusion policy, the age of a child will be defined as individuals under 18 years old instead of under 21 years old."*

4. Controlled Substances

Persons who handle controlled substances or dangerous drugs for the purpose of conducting research, and who are not registered as a pharmacy, drug wholesaler, distributor, supplier or medical practitioner, must register biennially with the Board of Pharmacy and obtain a drug researcher permit. Official Code of Georgia Annotated 26-4-49. The registered person must maintain accurate records of purchase, receipt, use, and disposal of the drugs for at least two years. Ga.Code 26-4-49. A copy of the researcher's controlled substances permit may be requested by the Office of Research Integrity Assurance in some situations.

5. Phase II and III Cancer Clinical Trials for Minors

All State health plans in Georgia must reimburse the patient's "routine care" costs associated with a dependent child's participation in a phase II or phase III cancer clinical trial that is testing prescription drugs. The child has to have been diagnosed with cancer prior to their 19th

birthday, and the trial has to have been approved by FDA or NCI. Ga. Code 33-24-59.1.

An approved clinical trial program under Ga. Code 33-24-59.1 is defined as a clinical trial that:

- Tests new therapies, regimens, or combinations thereof against standard therapies or regimens for the treatment of cancer in children;
- Introduces a new therapy or regimen to treat recurrent cancer in children; or
- Seeks to discover new therapies or regimens for the treatment of cancer in children which are more cost effective than standard therapies or regimens; and
- Has been certified by and utilizes the standards for acceptable protocols established by the:
    - Pediatric Oncology Group;
    - Children's Cancer Group; or
    - The Commissioner may otherwise define such term by rule and regulation after due notice, any required hearing, and compliance with any other requirements of applicable law, but only providing for such definition in a manner at least as restrictive as that established in this Code section.

6. Drug Investigation Laws

Investigational drugs may be used by scientific experts provided the drug is labeled "For Investigational Use Only." Official Code of Georgia Annotated 26-3-10. For outpatient clinics and hospital pharmacies, an investigational drug shall be administered under the direct supervision of the Principal Investigator or authorized clinician, with prior approval by a hospital committee, in accordance with an approved protocol and informed consent. Nurses shall be educated before administering the drug. The pharmacy shall maintain information on the drug. Patient confidentiality shall be maintained. Ga. Comp. R. & Regs. 480-13-.09, Ga. Comp. R. & Regs. 480-33-.09.

7. Medical and Other Records Privacy

Any hospital, health care facility or other organization rendering patient care may provide information, reports, statements, memoranda or other data relating to the condition and treatment of any person to research groups approved by the medical staff of the institution, to be used in any

study to reduce morbidity or mortality rates so long as the identity of the patient remains confidential. Official Code of Georgia Annotated 31-7-6.

Vital records may be disclosed for research purposes. Ga.Code 31-10-25.

Physicians, hospitals and health care facilities are not required to release raw medical data used in research except where authorized by law or by the patient or guardian. Ga.Code 24-9-40. The legislature declares that protecting the confidentiality of research data is essential to safeguarding the integrity of research. Defines "confidential raw research data" as that provided in support of a study approved by an oversight committee of a hospital, health care facility or educational institution, where the subjects' identities will not be material to the results, and will not be disclosed except to the subject or with the subject's written authorization or to a research sponsor. Ga.Code 24-9-40.2. Records must be furnished within a reasonable period of time to the patient, a provider designated by the patient or any other person designated by the patient. Ga.Code 31-33-2. Fees for search, retrieval and other direct administrative costs related to the provision of patient records established; may be adjusted annually by the state Office of Planning and Budget in accordance with the medical component of the consumer price index. All records remain the property of the provider. Ga.Code 31-33-3.

8. STD Reporting

HIV/AIDS information is confidential and shall not be disclosed except with the patient's consent. Physicians may inform the spouse, sexual partner or child if they are at risk of being infected and the physician attempted to notify the patient of the disclosure. Official Code of Georgia Annotated 24-9-40.1, Ga. Code 24-9-47. Health care providers, health care facilities or other persons who order an HIV test shall report each positive result to the Dept. of Health, along with information on patient's age, sex, race, address. Ga. Code 31-22-9.2. HIV tests may be ordered only after counseling the person, which may include information on AIDS, transmission, confidentiality, medical treatment. Ga. Code 31-22-9.2, Definitions Ga. Code 31-22-9.1. Minors may consent to treatment of STDs. Information may be given to or withheld from parents in the physician's judgment. Ga. Code 31-17-7. Any physician, hospital manager or other person who diagnoses or treats a case of venereal disease shall report it to the Dept. of Health. Ga. Code 31-17-2. Labs shall comply with reporting requirements for STDs unless operated exclusively for research purposes. Ga. Code 31-17-6, Ga. Code 31-22-9.

D. Health Insurance Portability and Accountability Act (HIPAA)

The Department of Health and Human Services' *National Standards to Protect the Privacy of Personal Health Information* are promulgated in the Health Insurance Portability and Accountability Act (HIPAA), commonly referred to as the "Privacy Act." This Act specifies requirements for protection of individually identifiable health information, or "protected health information" (PHI). See Section XXII of these policies, *"Health Insurance Portability and Accountability Act (HIPAA) for Protected Health Information,"* for a complete discussion of HIPAA and the procedures to comply at Georgia Tech.

E. Department of Defense, Incorporated by Addenda to Federalwide Assurance

An Addendum to Georgia Tech's Federalwide Assurance incorporates the Department of Defense's additional requirements for human subjects research involving the DOD. The Addendum documents Georgia Institute of Technology's assurance that it shall comply with the following laws, regulations, and guidance when conducting, reviewing, approving, overseeing, supporting, or managing DoD-supported research with human subjects:

- The Belmont Report
- Title 32 Code of Federal Regulations Part 219 (32 CFR 219), Department of Defense Regulations, "Protection of Human Subjects"
- Title 45 Code of Federal Regulations Part 46, (45 CFR 46) Department of Health and Human Services Regulations, "Protection of Human Subjects," Subparts B, C, and D as made applicable by DoDI 3216.02
- Title 21 Code of Federal Regulations 50, 56, 312, and 812, Food and Drug Administration (FDA) Regulations
- DoD Instruction (DoDI) 3216.02, "Protection of Human Subjects and Adherence to Ethical Standards in DoD-supported Research"
- Title 10 United States Code Section 980 (10 USC 980), "Limitation on Use of Humans as Experimental Subjects"
- DoDI 3210.7, "Research Integrity and Misconduct"
- DoDI 6200.02, "Use of Investigational New Drugs in Force Health Protection"
- Department of the Army
    - AR 70-25 Use of Volunteers as Subjects of Research, 25 January 1990
    - AR 40-38, Clinical Investigation Program, 1 September 1989
    - AR 40-7, Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances, 4 January 1991
- Department of the Navy
    - SECNAVINST 3900.39E of 29 May 2018
- Department of the Air Force
    - Air Force Instruction 40-402, Protection of Human Subjects in Research

- Office of the Secretary of Defense for Personnel and Readiness
  - HA Policy 05-003
- National Geospatial Intelligence Agency
- National Security Agency
- Defense Intelligence Agency
- Defense Threat Reduction Agency
- Defense Advanced Research Projects Agency
- United States Joint Forces Command
- Any other applicable requirements.

Appendix 15 sets forth the Department of Defense requirements in greater detail.

IV. Federalwide Assurance and Administration of Georgia Tech Program of Human Research

Reviewed: July 2024

The Georgia Institute of Technology IRB is constituted in accordance with federal regulations, are registered with the Office for Human Research Protections (OHRP), and hold a Federalwide Assurance. The Board is supported by the Office of Research Integrity Assurance, which reports to the Associate Vice President for Research Integrity Assurance.

A. Federalwide Assurance

Georgia Institute of Technology holds a Federalwide Assurance (FWA) of Compliance (number 00001731) with the Office for Human Research Protections (OHRP). A fully executed copy of Georgia Tech's Assurance is maintained by the Director of the Office of Research Integrity Assurance. The Georgia Institute of Technology Institutional Review Board is registered with the Office for Human Research Protections under number IRB00000548.

Georgia Institute of Technology applies its Federalwide Assurance and the Institutional Review Board *Policies & Procedures* to all human subjects research conducted by Georgia Tech faculty, staff, and students, regardless of whether the research activity is funded. Also included is any research for which an Assurance or another formal agreement (e.g., Interinstitutional Agreement) identifies the Georgia Tech Institutional Review Board as the IRB of record.

The Georgia Institute of Technology Institutional Review Board approval is required in advance for all projects with human subjects, regardless of whether the project is funded, and regardless of whether it is a subgrant or subcontract to or from another institution. (On occasion, reliance by the Ga Tech IRB upon another assured IRB may constitute the aforementioned approval; any such reliance must be approved by the Institutional Official).

1. Department of Defense Addendum to Federalwide Assurance

The Georgia Institute of Technology signed an Addendum to its *Federalwide Assurance (FWA) for the Protection of Human Subjects*,

agreeing to apply the Department of Defense (DOD) regulations and policies for the protection of human research participants when conducting, reviewing, approving, overseeing, supporting or managing DOD supported research with human subjects. The Addendum is applicable to Georgia Tech researchers conducting human subjects research supported by, or in collaboration with, or otherwise involving the Department of Defense. Human Subjects Research involves the DOD when any of the following apply:

- The research is funded by a component of the DOD (Navy, Army, Air Force, DARPA, etc);
- The research involves cooperation, collaboration, or other type of agreement with a component of DOD;
- The research uses property, facilities, or assets of a component of DOD; or
- The subject population will intentionally include personnel (military or civilian) from a component of DOD.

See Appendix 15 for guidance on satisfying the DOD requirements.

B. Institutional Review Board at Georgia Institute of Technology

One Institutional Review Board is established at Georgia Tech. The Central IRB (IRB00000548) reviews all human subjects research activities taking place at Georgia Tech or where Georgia Tech investigators are engaged in the human subjects research. Exceptions can be made per specific agreement where the Central IRB can rely on another IRB's approval. These policies apply to the Central IRB, with some notable exceptions. Additionally, anyone proposing to conduct classified research involving human subjects should consult the Office of Research Integrity Assurance.

The IRB was established pursuant to *Title 45 Code of Federal Regulations Part 46* including *Subparts A, B, C, and D*, and *Title 21 Code of Federal Regulations Part 56*. The IRB is sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB is able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB therefore includes persons knowledgeable in these areas. IRBs that regularly review research involving a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, shall include one or more individuals knowledgeable about and experienced in working with these subjects.

C. Institutional Official

Federal regulations require that there be a point of responsibility within the institution for the oversight of research and IRB functions. This point should be an official of the institution who has the legal authority to act and speak for the institution, and should be someone who can ensure that the institution will effectively fulfill its research oversight function. The institution's president shall appoint or delegate the appointment of the individual. The President of Georgia Institute of Technology has delegated this authority through the Executive Vice President for Research to the Associate Vice President for Research Integrity Assurance (AVP-RIA).

The Associate Vice President for Research Integrity Assurance also serves as the Institutional Official (IO) and has the authority to legally commit Georgia Institute of Technology to meet federal regulatory requirements. The Institutional Official is responsible for appointing the Chair of the Georgia Institute of Technology Institutional Review Board and its members. As Institutional Official, the AVP-RIA signs Georgia Institute of Technology's Federalwide Assurance. The Institutional Review Board reports to the IO.

D. Office of Research Integrity Assurance

The Office of Research Integrity Assurance provides administrative support to the Institutional Review Board. The Office of Research Integrity Assurance reports to the Associate Vice President for Research Integrity Assurance/Institutional Official (AVP-RIA/IO) and through the AVP-RIA/IO to the Office of the Executive Vice President for Research. While the AVP-RIA/IO generally attends all meetings of the IRB, it is the responsibility of the Office of Research Integrity Assurance to keep the AVP-RIA/IO informed of IRB activities by providing meeting minutes and by frequent interaction and consultation.

The university's Federalwide Assurance and Registration are maintained by the Office of Research Integrity Assurance.

In close coordination with the Board, the Office of Research Integrity Assurance facilitates ethical conduct of research through advance and continuing protocol review; monitoring and reporting; convening regular meetings for review of proposed and continuing research; and providing educational programs for faculty, staff, and students. The Office of Research Integrity Assurance oversees the development and implementation of policies, procedures, and educational programs which satisfy the many regulations governing the conduct of such research.

1. Official Institute Records Maintained by Research Integrity Assurance

Federal regulations set forth specific record keeping requirements for the institution and the IRB. Adequate documentation of IRB activities must be prepared and maintained. In addition to the written IRB procedures and membership lists required by the Assurance process, such documentation must include copies of all research proposals reviewed, minutes of IRB meetings, records of continuing review activities, copies of all correspondence between the IRB and investigators, and statements of significant new findings provided to subjects.

Minutes of IRB meetings must be kept in sufficient detail to record the following information: attendance at each meeting; actions taken by the IRB; the vote on actions taken (including the number of members voting for, against, and abstaining); the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution. Meeting minutes are retained for at least three years after closure of all protocols cited therein.

Individual protocol records are retained for at least three years after completion of the research. All records must be accessible for inspection and copying by authorized representatives of the department or agency supporting or conducting the research at reasonable times and in a reasonable manner. Such records must also be reasonably accessible to federal auditors.

The university's repository of official Institutional Review Board records is maintained by the Office of Research Integrity Assurance and includes the following:

- The Federalwide Assurance and Addenda thereto
- Records of Registration filed with the Office for Human Research Protections, NIH, PHS
- Current rosters of Georgia Tech IRB membership and credentials
- IRB *Policies & Procedures*
- Minutes of meetings, including information regarding member attendance, discussions held, decisions made, and voting results
- All materials submitted to the committee for initial and continued review of each study including: the Georgia Tech IRB applications, protocol, consent forms, adverse event reports, proposed amendments, progress reports, and all correspondence generated between the committee, the investigators, and sponsoring agencies.
- Documents approved by the IRB, including stamped consent forms and letters of approval
- Records of any non-compliance and resolution thereof.

Records are maintained in accordance with federal directives and Board of Regents, University System of Georgia, policy. Electronic records, it should be noted, are maintained indefinitely. (It is the responsibility of the investigator to maintain signed consent documents for three years after the project closes).

V. Institutional Review Board Membership and Operations

Reviewed: July 2024

Federal policy provides that IRBs must have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB must be sufficiently qualified through the experience and expertise of its members and the diversity of their backgrounds, including considerations of their racial and cultural heritage and their sensitivity to issues such as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

The membership of the Georgia Tech IRB is constituted in accordance with federal regulations, and board meetings are conducted in compliance with those directives.

A. IRB Membership Appointments

The IRB has at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The authority to appoint board members has been delegated by the President of the Georgia Institute of Technology through the Executive Vice President for Research to the Institutional Official. Members of the Georgia Tech IRB are appointed by the Institutional Official with consideration given to recommendations from Deans, Chairs, current IRB members, the Director of Research Integrity Assurance, and/or members of the community. Members are generally appointed initially for a one year term, although some members serve for several terms. All members have full voting rights. The IRB Chair is appointed by the Institutional Official. A Vice Chair may be elected by the IRB members.

1. Alternate Members of the Board

Alternate members may be appointed to serve in the absence of regular members. Alternates must have expertise similar to that of the regular member whom he/she replaces; that is, a *non-scientist alternate* may not replace a *scientist member*. The appointment process is the same as for regular members of the IRB, and alternates' names are included in the

IRB's official membership roster. Alternate members' terms of service are virtually the same as those of regular members. They receive training and orientation for IRB service in the same way as regular members. Alternate member(s) also have electronic access to the agenda and associated items well in advance of scheduled IRB meetings. Alternates are encouraged to attend as many meetings as possible, even when not required to be present to act as a formal alternate.

Alternate members review and vote on protocols at convened meetings only when the regular member for whom they are substituting is absent or recuses oneself. The IRB minutes document meetings at which the alternate member serves in place of the regular member. When an alternate member substitutes for a regular member, the alternate member's vote counts towards the quorum in the same way as the regular member's vote. IRB meetings will not be conducted if alternates constitute the majority of the members present.

2. Nondisclosure of Research Materials and Protocols

While members (and alternate members) of the Institutional Review Board are ethically bound to respect confidentiality of research materials submitted for their review, all members (and alternate members) sign nondisclosure agreements. Georgia Tech employees sign such agreements at the time of employment, and community members sign them when appointed to the Board.

3. Liability Coverage for IRB Members

Since the Georgia Tech IRB is a constituted committee of the Georgia Institute of Technology, liability coverage (excluding personal liability coverage) is provided by the Institute for members (and alternate members) serving on the committee and performing their duties in accordance with Institute policy.

B. Education of Institutional Review Board Members

The Office of Research Integrity Assurance conducts an orientation for new members in which relevant materials are provided (Belmont Report, federal regulations, Georgia Institute of Technology *Policies & Procedures*), and the details concerning committee function and procedures are discussed. Board members are also provided training on use of the electronic proposal submission and tracking tool. Board members are provided the opportunity to attend professional conferences in order to stay informed about changes in federal guidance related to human subjects protections. Members are expected to complete online training via Collaborative Institutional Training Initiative

(CITI) at the time of their appointment and thereafter as required by Georgia Institute of Technology's IRB Policy and Procedures.

C. Meetings

1. IRB Meeting Schedule

The Central IRB generally meets monthly on the third Friday of the month, depending on the holiday schedule and whether there are matters to consider. Additional meetings will be called if necessary for the Board to fulfill its responsibilities.

2. Quorum

A meeting quorum is a majority of the voting members (fifty percent plus one), including at least one member whose primary concerns are in nonscientific areas. When the quorum fails because attendance falls below a majority due to recusal of members with conflicting interests or early departures, or absence of a nonscientist member, no further actions or votes may be taken.

3. Conflict of Interest Related to Proposed Research

No Georgia Tech IRB member or alternate participates in the review of any study on which the or a member of the member's family is an investigator, has a personal or professional interest (e.g., the member's Georgia Tech performance, promotion, or tenure assessment could be affected by the protocol), or where a potential for conflict of interest exists. Members who have such a conflict of interest must leave the room during deliberation and vote. For the purposes of this section "Family" means spouse or partner, dependents [as defined in O.C.G.A. 45-10-20], and anyone who could reasonably be assumed to be family in the context of situations in which there may be the appearance of a Conflict of Interest.

4. Use of Telecommunications for IRB Meetings

Through use of telecommunications (e.g., telephone- or video-conferencing), Georgia Tech's IRB may conduct official business without all members physically present. In this case, the following criteria must be met:

The forum allows for real time verbal interaction equivalent to that occurring in a physically-convened meeting (i.e., members can actively and equally participate, and there is simultaneous communication). All members are given advance notice of the meeting; documents normally provided to members during a physically-convened meeting are provided to all members in advance of the meeting; all absent members must have access to the documents and the technology necessary to fully participate; a quorum of voting members is convened; and if a vote is

called for, the vote occurs during the meeting and is taken in a manner that ensures an accurate count of the vote. Written minutes of the meeting are maintained in accordance with the PHS Policy.

A mail ballot or individual telephone polling cannot substitute for participation in a convened meeting. Opinions of absent members that are transmitted by mail, telephone, fax or e-mail may be considered by the convened IRB members but shall not be counted as votes.

D. Consultation with Experts

The Georgia Institute of Technology IRB may, at its discretion, invite consultants with competence in special areas to assist in the review of complex issues requiring expertise beyond, or in addition to, that available on the committee. The consultant may attend meetings to present information and to take questions but does not participate in the deliberation or vote.

E. Visitors at IRB Meetings

Occasionally, visitors will attend IRB meetings. Unless the visitor is a Georgia Tech employee with a current and relevant Non-Disclosure Agreement (NDA) in place, the visitor will be required, in advance of the meeting, to sign a NDA prepared by the Office of Research Integrity Assurance. Investigators may be invited to attend the IRB meetings to clarify issues concerning their proposed research activity and to take questions from the board. Visitors must leave the room during the board's deliberation and vote. Of course, visitors do not count toward quorum.

VI. Eligibility for the Title of Principal Investigator on Protocols

Reviewed: July 2024

A. Eligibility for Title of Principal Investigator on Protocols

The term "Principal Investigator" refers to the single individual who shall have full and final responsibility for the conduct of a protocol (research study) involving human subjects. For IRB purposes, the title of Principal Investigator (PI) or co-Principal Investigator (co-PI) will be allowed when the individual is a current member of the Georgia Tech academic or research faculty as defined in the faculty handbook, or when the individual satisfies one of the exceptions specified below. Clinical investigators, regardless of their role(s) in the study, shall hold the appropriate current medical and/or state/federal licenses.

Academic faculty designations include varying levels of professor, professor of the practice, academic professional, archivist, librarian, lecturer and senior lecturer, and instructor. Also included in this category are the president, provost, vice provosts, executive vice president for research, executive vice president for administration and finance, college deans, dean of the libraries, dean of students, school chairs, and the registrar.

Research faculty include varying levels of regents researcher, research associate, research engineer, research scientist, research technologist, and extension professional. Others included are the president, provost, executive vice president for research, executive vice president for administration and finance, and director – research (as the term is used for GTRI lab directors).

Retirees: If the proposed PI or co-PI is retired and working on an hourly-as-needed basis, there must be at least one School, Laboratory, or Department willing to provide the necessary administrative commitment to permit the protocol to be carried out. This arrangement must be documented in writing in the protocol.

Postdoctoral Fellows may serve as PI or co-PI if the relevant department head signs off on the protocol. This includes Brittain Fellows.

Adjunct faculty may not serve as PI or co-PI on an IRB protocol *unless they are also eligible to be a PI as described above*. They may hold the title of co-investigator if they sign a Visiting Scholar Agreement. (Some personnel are faculty in the Georgia Tech Research Institute and also adjunct in an academic unit; some personnel may be faculty in one academic unit and adjuncts in another).

Affiliates may not be named as PI or co-PI.

Non-employees are not generally eligible to serve as a PI or co-PI on protocols. Requests for exceptions for a non-employee to serve as PI or co-PI on a specific protocol for a limited time may be directed to the Institutional Official for Research. This exception is generally appropriate for newly hired faculty in transition from another institution and enables research to continue with minimal interruption.

Occasionally, an individual who is not otherwise eligible for the title of PI or co-PI may receive an exception letter from the Institutional Official, as described in item B., below. Some students may also qualify under D. 1 or 2, below.

B. Additional Principal Investigator Credentials Required by FDA

For studies subject to the Food & Drug Administration regulations, investigator credentials including, if applicable, license to practice medicine, must be verified by the Institutional Review before IRB approval can be given. Companies and medical practices must also provide copies of their business licenses.

If conducting drug/pharmaceutical studies, investigators must also review, date, and sign the *FDA Guidance on Investigator Responsibilities*. (See Appendix 19, *FDA Guidance for Sponsors, Clinical Investigators, and IRBs Regarding FDA Form 1572)* and the Frequently Asked Questions on the FDA Form 1572 (*See Appendix 19, FDA Guidance for Sponsors, Clinical Investigators, and IRBs Regarding FDA Form 1572).*

C. Exceptions Requiring Approval by the Institutional Official

Exceptions to the general eligibility requirements for designation as Principal Investigator will be considered upon submission of a written request to the Institutional Official. The request should justify why the individual should be designated as the Principal Investigator and must be signed by the appropriate departmental representative (Chair, Director, or Department Head). A copy of the approved exception, signed by the Institutional Official and the requesting department's head, must be provided to the Office of Research Integrity Assurance before a protocol will be approved.

D. Eligibility Exceptions for Graduate and Undergraduate Students as Principal Investigators

Usually, graduate and undergraduate students are named as Co-Investigators, as this title designates key personnel but does not have the oversight responsibilities of a Principal Investigator. Exceptions to allow graduate and undergraduate students to use the title of Principal Investigator on an IRB protocol are described below.

1. Exception for Georgia Tech Students Receiving Stipends and Tuition in Support of Their Work on Emory Protocols

In those few cases where the Principal Investigator is a faculty member at Emory University, AND no Georgia Tech faculty member has any involvement in the project, AND the funding (if any) is awarded to Emory University with a subcontract to Georgia Tech solely for the student's stipend and tuition, AND a Georgia Tech student is being mentored and supervised by the Emory University Principal Investigator, the Georgia Tech student will be named Principal Investigator (PI) for Georgia Tech's tracking purposes.

In addition to completing the required training modules in human research protections, the student must be named in the approved Emory protocol, AND the only funding from Emory University to Georgia Tech must be for the student's stipend and tuition.

The Georgia Tech student PI must submit to the Georgia Tech Office of Research Integrity Assurance:

- A copy of the approved Emory IRB protocol;
- A copy of the Emory IRB letter of approval;
- The protocol title must start with the word EMORY; and
- The funding source must be clearly identified.

The Student PI must meet with a Research Associate in the Georgia Tech Office of Research Integrity Assurance for a brief overview of PI responsibilities before a letter of approval will be issued to the student from the Georgia Tech IRB.

2. Exception for Georgia Tech Students Receiving Fellowships Supporting Their Work on Emory Protocols

In those few cases where the Principal Investigator is a faculty member at Emory University, AND no Georgia Tech faculty member has any involvement in the project, AND a Georgia Tech student is being

mentored and supervised by the Emory University Principal Investigator, AND the funding awarded to Georgia Tech is solely for the student's fellowship, the Georgia Tech student can be named Principal Investigator (PI) for Georgia Tech's tracking purposes.

In addition to completing the required training modules in human research protections, the student must be named in the approved Emory protocol, AND the only funding from Emory University to Georgia Tech must be for the student's fellowship.

The Georgia Tech student PI must submit to the Georgia Tech Office of Research Integrity Assurance:

- A copy of the approved Emory IRB protocol;
- A copy of the Emory IRB letter of approval;
- The protocol title must start with the word EMORY; and
- The funding source must be clearly identified

The Student PI must meet with a Research Associate in the Georgia Tech Office of Research Integrity Assurance for a brief overview of PI responsibilities before a letter of approval will be issued to the student from the Georgia Tech IRB.

3. Exception for Georgia Tech Biomedical Engineering Students Conducting Research on Emory Led and Supervised Protocols

Georgia Tech Biomedical Engineering (BME) students working on an Emory University IRB-approved research protocol under the supervision of an Emory University faculty advisor are not required to submit a separate application to the Georgia Tech IRB when all the following conditions are met:

- The research is being conducted under an Emory University IRB-approved protocol.
- The student's research activities are performed under the oversight of an Emory University faculty advisor who is listed on, or covered by, the Emory-approved protocol.
- Georgia Tech is not the recipient of federal funding supporting the research.
- The student is conducting research activities solely within the scope of the approved Emory IRB protocol.
- The student must contact the Georgia Tech IRB Reliance Team and provide:
    - The Emory IRB approval letter
    - The approved research protocol

- Any approved consent, assent, parental permission, recruitment, or other participant-facing documents, as applicable
- A description of the student's role on the project, including the specific human subjects research activities in which the student will be engaged
- The student must provide documentation of current, applicable CITI training required for the research and confirm that they do not have a financial or other disclosable conflict of interest related to the study.

If any of these conditions are not met, review and approval by the Georgia Tech IRB may be required before the student may engage in human subjects research activities.

Note: Students should consult with the Georgia Tech IRB Reliance Team if there is any uncertainty regarding funding sources, training requirements, conflict of interest considerations, the scope of approved research activities, or the need for Georgia Tech IRB review.

E. Circumstances That Render Researcher Ineligible to Hold Role of Principal Investigator, Co-Principal Investigator, or Investigator

At initial and continuing review, the Institutional Review Board shall consider whether *any* study personnel fits any condition of the following:

- If involved in an investigation or other research that was terminated, an explanation of the circumstances leading to termination must be provided. (21 CFR 812.43(c)(3)
- Has been debarred.
- Has a restriction, limitation, judgment on his license or its status (if a license is applicable to that person).
- Has any prior regulatory inspection history that resulted in an official written citation, such as an FDA warning letter.

F. Definitions

1. Principal Investigator

This title identifies the individual responsible for the conduct of the study. This responsibility includes the conduct of the study, all administrative aspects, and the study's adherence to relevant policies and regulations (institutional, state and federal).

2. Co-Principal Investigator

This designation refers to individuals who share the responsibility for the study with the Principal Investigator and therefore requires the same qualifications as for PI.

3. Co-Investigator
This title designates key personnel for a project, but without the oversight responsibility of a Principal Investigator. Individuals do not need to meet the qualifications of PI under this policy to be named a Co-Investigator, but should be key personnel on the project. For example, a Master's or PhD student submitting their dissertation for IRB approval may be listed as the Co-investigator. The thesis or dissertation chair/advisor should be listed as the PI on the IRB application. An undergraduate working on a senior thesis or other class research project should list oneself as the Co-investigator. The faculty member who is advising the student on the research should be listed as the PI for IRB purposes.

In addition, faculty members may be listed as Co-Investigators if their role on the study is not that of PI or Co-PI.

VII. Categories of Review: Exempt, Expedited, Full Board

Reviewed: July 2024

Research involving human research participants will fall into one of three review categories: exempt, expedited, or full board. Each category is defined and discussed below. The IRB will make a final determination as to the correct review category of all protocols submitted.

A. Exempt Review Research

Many social, behavioral and educational studies involve little or no risk to participants. Research of existing data, medical records, and pathological specimens also usually present little risk to subjects, particularly if identifiers are removed from the data. While subjects' rights and welfare must still be protected, the federal regulations permit less detailed scrutiny by the Institutional Review Board in most studies of these kinds. Research in this category is considered *exempt from further committee review*. However, federal regulations require a determination of exemption be made *not by the Principal Investigator* but by someone authorized appointed by the Institution. Therefore, the Georgia Tech IRB requires that such activities be on file with the Office of Research Integrity Assurance and that they be determined to be *exempt* by an experienced staff member of the Office of Research Integrity Assurance or other voting member of the IRB.

1. Special Considerations

Certain populations have special protections, as outlined in Subparts B, C, D of *§45CFR46. Please see a description of the populations and how the Exempt categories apply to each population. See §45CFR46, Subpart B:* Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research; *Subpart C*: Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects, and *Subpart D*: Additional Protections for Children Involved as Subjects in Research.

a. Pregnant Women, Fetuses, and In Vitro Fertilization (Subpart B)

Research that involves pregnant women, fetuses, and in vitro fertilization (Subpart B) may be eligible for exemption from further committee review if the conditions of the exemption are met.

b. Prisoner Research (Subpart C)

The exemptions in this section do not apply to research involving prisoners, except for research aimed at involving a broader subject population that only incidentally includes prisoners.

c. Children (Subpart D)

The exemptions at paragraphs (d)(1), (4), (5), and (6)of this section may be applied to research involving children if the conditions of the exemption are met. Paragraphs (d)(2)(i) and (ii) of this section only may apply to research subject to subpart D involving educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed. Paragraph (d)(2)(iii) of this section may not be applied to research subject to subpart D.

2. Exempt Review Categories

a. Exempt Categories 1-6

The Department of Health and Human Services has identified certain categories of research involving human subjects that qualify for exemption from certain federal regulations applicable to research. At Georgia Tech, the IRB makes federal exemption determinations (categories 1-6) according to 45 CFR 46.104

1. Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
2. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public

behavior (including visual or auditory recording) if at least one of the following criteria is met:
(i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).
3. (i) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:
(A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
(B) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
(C) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).
(ii) For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

(iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of “health care operations” or “research” as those terms are defined at 45 CFR 164.501 or for “public health activities and purposes” as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under

those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.
(i) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.
6. Taste and food quality evaluation and consumer acceptance studies:
(i) If wholesome foods without additives are consumed, or
(ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

b. FLEX Categories 2 and 3

In the case of non-federally funded human research, Georgia Tech has created additional Flexible Exemption categories.

For the following non-Federal flexible exemption categories, the research must meet the following criteria in addition to all specifications of the exemption category:

- Research is not subject to FDA regulations.
- Research is not federally funded.
- Research is not contractually or otherwise subject to federal research requirements, including but not limited to research conducted under the Department of Veterans Affairs or under an NIH Certificate of Confidentiality.
- Research does not involve prisoners as participants.

- Research meets Georgia Tech's ethical standards governing the conduct of the research, including appropriate provisions for the protection of privacy and confidentiality when identifiable and coded information are used.

Flex Exempt 2
Minimal risk research that is not federally funded; Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:
(i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to determine that, when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

NOTE: This category may be applied to studies involving minors only if they are enrolled Georgia Tech students

FLEX Exempt 3
Minimal risk research that is not federally funded involving benign behavioral interventions and/or gentle physical movement in conjunction with the collection of information from a subject through verbal or written responses (including data entry), audiovisual recording, or use of non-invasive commercially available measurement technology or tools (excluding MRI, fMRI, TMS). The participant must prospectively agree to the intervention and information collection and at least one of the following criteria must be met:
(A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(B) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
(C) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects and, when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

NOTE: This category may be applied to studies involving minors only if they are enrolled Georgia Tech students

Once a determination of exemption has been made, the investigator will be notified in writing. The full Institutional Review Board is to be informed of all protocols reviewed and determined to be exempt. The responsibility for this communication lies with the Office of Research Integrity Assurance.

3. Exempt Review Submission Process

To request for Exempt Review Determination, the PI must submit to the IRB in IRB Wise. When submitting, the PI will need to complete Section I. "General Information," Section II. "Research Design and Methodology" question N (only if funded), Section III. "Subject Information, Consent and Types of Studies" question E (only if you are obtaining an identifiable dataset or identifiable human specimen), Section IV. "Studies involving Department of Defense, Radiation, or Nanotechnology," upload all of the study documents to Section VI. "Attach Documents," and complete the "Conflict of Interest" section. More information may be requested and additional sections within IRB Wise may need to be completed due to the specifics of the study.

Please note that all documents, including but not limited to funding proposals, consent, recruitment, data collection instruments (e.g., surveys, interview guides, etc.) are needed in the submission to confirm the study qualifies for exempt review. For exempt research that involves interaction with subjects, there usually should be a process to ask subjects to participate and confirm their agreement. However, signed consent is not required for most exempt research, and the consent process and documents can be much simpler than those required for non-exempt research.

B. Expedited Review Categories

The Department of Health and Human Services and the Food and Drug Administration regulations governing protection of human subjects recognize that full Institutional Review Board review is not necessary for every protocol. Hence, certain types of research may be reviewed and approved under an *expedited* procedure. When allowable, expedited approvals may be granted by the Institutional Review Board Chair or any other IRB members designated by the Chair. Reviewers may exercise all authority of the IRB, except that no individual member, including the Chair, may disapprove a research protocol. Any proposed disapproval is to be referred to the full board for review and disposition.

In order to qualify for expedited review, research activities must present no more than minimal risk to human subjects and involve only procedures listed in one or more of the nine categories listed below. The categories in this list apply regardless of the age of subjects, except as noted. The expedited review procedure is not permitted when identification of the subjects and/or their responses would reasonably place subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. Categories one (1) through seven (7) below pertain to both initial and continuing IRB review, while categories (8) and (9) apply in certain cases to research already approved by the full board.

1. Clinical studies of drugs and medical devices only when the following conditions are met:
    (a). Research on drugs for which an investigational new drug application is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.) AND
    (b). Research on medical devices for which an investigational device exemption is not required, OR the medical device is cleared/approved for marketing and is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
    (a). from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
    (b). from other adults and children (persons under 18 years old) considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in

an 8 week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means. Examples:

(a). Hair and nail clippings in a non-disfiguring manner;

(b). deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;

(c). permanent teeth if routine patient care indicates a need for extraction;

(d). excreta and external secretions (including sweat);

(e). uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue;

(f). placenta removed at delivery;

(g). amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;

(h). supra- and sub gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;

(i). mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;

(j). sputum collected after saline mist nebulization.

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples:

(a). Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;

(b). weighing or testing sensory acuity;

(c). magnetic resonance imaging;

(d). electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;

(e). moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (Note: See

section I.a. for similar research that may fall into the exempt category. This listing refers only to research that is not exempt.)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (Note: See section I.A. for similar research that may fall into the exempt category. This listing refers only to research that is not exempt.)

8. Continuing review of research previously approved by the full committee as follows:

(a). Where:

(i). the research is permanently closed to the enrollment of new subjects;

(ii). all subjects have completed all research-related interventions; and

(iii). the research remains active only for long-term follow-up of subjects; or

(b). Where no subjects have been enrolled and no additional risks have been identified; or

(c). Where the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the Georgia Tech IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Once an expedited review has been completed, the investigator will be notified regarding the status of the application. This written notification will indicate whether the application was fully approved, required modifications/clarifications in order to secure approval, or deferred for full committee review. The full Institutional Review Board is to be informed of all protocols reviewed and approved under the expedited review process. The responsibility for this communication lies with the Office of Research Integrity Assurance staff, some of whom are members of the Institutional Review Board and conduct expedited reviews.

NOTE: Studies intended to evaluate the safety and effectiveness of a medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications. Studies of medical devices not cleared or

approved for marketing by the Food & Drug Administration are also not eligible for expedited review.

C. Full Board Review

Protocols presenting greater than minimal risk, or that otherwise do not qualify for review under exempt or expedited procedures, must be reviewed by the full Institutional Review Board at a convened meeting. The current schedule of deadlines and meeting dates is posted at http://www.oria.gatech.edu.

Protocols to be reviewed by the full board are distributed to members in advance of the meeting. After the meeting, the investigator is notified regarding the IRB's determination. The Board may determine to approve the protocol, require clarifications or modifications in order to secure approval, defer the protocol (that is, the investigator's response must be considered at another meeting of the full board), or disapprove the protocol outright. The IRB determination is generally communicated in writing to the Principal Investigator by the Office of Research Integrity Assurance.

VIII. Deciding Whether Institutional Review Board Approval Must Be Obtained

Reviewed: July 2024

Prior IRB approval must be obtained in advance for *any research activity* that either meets the Department of Health & Human Services (DHHS) definition of research that involves humans as subjects or the Food and Drug Administration (FDA) definition of a *clinical investigation* that involves human subjects. This requirement includes any proposed research activity conducted by Georgia Tech faculty, staff, or students and that involves contact with live persons OR identifiable biological specimens. Some exceptions to this policy are listed at the end of this section.

A. Research Activities That Require IRB Approval

If the answer is *yes* to the two following questions, the activity must be submitted to the IRB for review prior to initiation of the activity:

- Is the activity a systematic investigation including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge?
- Does the activity involve living individuals about whom the investigator obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens?

If the answer is *yes* to any of these three questions, the activity must be submitted to the IRB for review prior to initiation of the activity.

- Does the activity involve the use of a drug (including an approved drug or an over-the-counter drug), other than the use of an approved drug in the course of medical practice?

- Does the activity involve the use of a medical device (including an approved medical device), other than the use of an approved medical device in the course of medical practice? (Medical devices generally include devices intended for use in diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease,

in humans or other animals, and devices intended to affect the structure or any function of the body of humans or other animals.

- Will data be submitted to the FDA or held for their inspection?

A determination as to whether the activity constitutes human subjects research will be made by a member of the IRB.

1. Review Required Under Department of Health and Human Services (DHHS) Regulations

The Department of Health and Human Services (DHHS) is responsible for implementing the regulations at §45CFR46 governing biomedical and behavioral/social science research involving human subjects. DHHS regulations define *human subject* as a living individual about whom an investigator conducting research obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. *Intervention* includes both physical procedures by which information or biospecimens are gathered and manipulations of the subjects' environment that are performed for research purposes. Intervention includes venipuncture, surveys, questionnaires, and focus groups, human factors, behavioral observations, and more. *Interaction* includes communication or interpersonal contact between investigator and subject. *Private Information* is that information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the Investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. This definition may include identifiable private information obtained from a primary subject about a third party ("secondary subject"). DHHS defines research as any systematic investigation including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities must be *systematic* to be considered research and include those involving predetermined methods for answering a specific question, testing hypotheses or theories, and may include interviews, program evaluations, and observational studies. Activities must contribute to *generalizable knowledge* or be intended to extend beyond a department

or internal use. Generally, a thesis and a dissertation are considered research for IRB purposes.

Another research activity that involves human subjects is ethnographic research, wherein the investigator will participate, overtly or covertly, in people's daily lives for an extended period of time. The investigators watch what happens, listens to conversations, asks questions and collects additional data to create a broader understanding of a particular environment, ethnic group, gender, and so on.

Internet Research frequently employs online questionnaires and surveys, surveys, "chat rooms", and other web-based interactions. Any expectation of privacy should be addressed in designing studies of this type.

The regulations extend to the use of human organs, tissue, and body fluids from individually identifiable human subjects. The use of autopsy materials is not regulated by §45CFR46 and is not subject to IRB review.

2. Review Required Under Food and Drug Administration (FDA) Regulations

The Food and Drug Administration (FDA) is responsible for implementing regulations governing the use of investigational drugs, biologics, devices, *in vitro* diagnostic devices, and radiological procedures including radioactive drugs in clinical investigations with humans.

The Food and Drug Administration (FDA) defines *human subject* as an individual who is or who becomes a participant in research either as a recipient of a test article or as a control. These studies are referred to as *clinical investigations* or *clinical trials*. A subject may be either a healthy individual or a patient. In the case of research involving medical devices, a human subject is a human who participates in an investigation either as an individual on whom—or on whose specimen—an *investigational device* is used, or as a control. FDA regulations further define human subjects as those persons who provide tissue specimens for testing the safety or efficacy of a device, even if the specimens have no identifying data. A *test article* is any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to FDA regulation. A clinical *investigation* is any experiment involving a test article and one or more human subjects as defined by FDA regulations *and* either of the following applies:

The study meets the prior submission requirements of FDA laws and regulations OR prior submission is not required but the experiment's

results are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

Clinical investigations include the following:

- Any use of a drug (approved or unapproved) except for the use of a marketed drug in the course of medical practice.
- Any research in which the use of a drug is specified by the protocol and is not left up to the judgment of a physician, it is a clinical investigation. For example, all oncology clinical trials of chemotherapy are clinical investigations even if all drugs are approved drugs.
- Activities to determine the safety or effectiveness of a medical device, such as the comparison of two diagnostic modalities.
- Activities where data will be submitted to or held for inspection by FDA, such as collection of data to support a submission to FDA for a health marketing claim for a health drink product.

When studies are FDA-regulated, they cannot be granted an exemption from IRB review, and consent may not be waived using the DHHS criteria. Industry-sponsored research involving surveys, interviews, educational tests, or existing data, documents, or specimens, should be carefully reviewed to determine whether the sponsor will submit the data to the FDA or want it held for later FDA inspection.

NOTE: The Georgia Tech Institutional Review Board will search current FDA Guidance when studies are reviewed to ensure that the review is in compliance with current Guidance. The IRB may consider any new or updated FDA (or Office of Human Research Protections) Guidance or Information Sheets in the review of studies.

3. Pilots and Feasibility Studies

In November of 2011, the FDA issued draft Guidance *"Investigational Device Exemptions for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies."* (See Appendix 21). Intended to encourage early-stage development of medical devices and promote early state development, the draft Guidance defines several types of clinical trials (early feasibility, first in human, traditional feasibility, and pivotal studies). Revised FDA policies regarding Investigational Device Exemptions for early feasibility studies are described in the draft Guidance. The FDA may now approve IDEs with less nonclinical data than usually required for traditional feasibility and pivotal studies.

Pilot studies (feasibility studies), even those involving only one or two individuals, are subject to the same scrutiny as a full scale research project and must have IRB approval prior to initiation. Pilots may be any one of the following:

a. An **Early Feasibility Study** is a limited clinical investigation of a device early in development, typically before the device design has been finalized, for a specific indication (e.g., innovative device for a new or established intended use, marketed device for a novel clinical application). It may be used to evaluate the device design concept with respect to basic safety and device functionality in a small number of subjects (generally fewer than 10 initial subjects) when this information cannot be readily provide through additional nonclinical assessments or appropriate nonclinical tests are unavailable. Information obtained from an early feasibility study may guide device modifications. An early feasibility study does not necessarily involve the first clinical use of a device.

Prior to Investigational Device Exemption (IDE) submission and to avoid preventable delays, it is advisable to contact FDA to determine whether the proposed investigation can be classified as an early feasibility study.

b. A **First in Human** (FIH) study is a type of study in which a device for a specific indication is evaluated for the first time in human subjects.

c. A **Traditional Feasibility Study** is a clinical investigation that is commonly used to capture preliminary safety and effectiveness information on a near-final or final device design to adequately plan an appropriate pivotal study. As compared to an early feasibility study, more nonclinical (or prior clinical) data are necessary for approval to initiate a traditional feasibility study; however, a traditional feasibility study does not necessarily need to be preceded by an early feasibility study.

d. A **Pivotal Study** is a clinical investigation designed to collect definitive evidence of the safety and effectiveness of a device for a specified intended use, typically in a statistically justified number of subjects. It may or may not be preceded by an early and/or a traditional feasibility study.

4. Other Activities That Require IRB Review

In addition to the foregoing, other types of research activities require prior Institutional Review Board approval, either under DHHS and/or FDA regulations.

- Innovative Procedures, Treatment, or Instructional Methods: A systematic investigation of innovations in diagnostic, therapeutic procedure, or instructional method in multiple participants in order to compare to standard procedure. The investigation is designed to test a hypothesis, permit conclusions to be drawn, and thereby develop or contribute to generalizable knowledge.
- Repositories of data or specimens: Preliminary activities typically designed to help the Investigator refine data collection procedures. A storage site or mechanism by which identifiable human tissue, blood, genetic material or data are stored or archived for research by multiple investigators or multiple research projects.
- Retrospective Data: Retrospective review of patients' medical records with the intent to report or publish the summary.
- Emergency use of an investigational drug or medical device: (*This situation is highly unlikely to arise on a study conducted in Georgia Tech facilities, given the typical human studies conducted by Georgia Tech faculty. Georgia Tech does not have a medical school, but does considerable collaboration with other medical colleges and hospitals).* When emergency use of a test article is initiated without prior IRB review and approval, under DHHS regulations the patient is not considered a research participant in a prospectively conceived research study. The data derived from the use of the test article may not be used to determine efficacy of the device but they may be used for safety data if any reportable event or product problem occurs during the emergency use.
- If the emergency care involves drugs, devices, or biologics that are considered to be investigational by the Food and Drug Administration (FDA), then it may be necessary to meet FDA requirements to use the investigational article for emergency purposes.
- Thus, the distinction for DHHS-supported or - conducted research is that while the physician may, without prior IRB approval, treat the patient/subject using a test article (if the situation meets the FDA requirements), the subject may not be considered a research subject; data derived from use of the test article may not be used in the study.
- Research Conducted by Students: Student-conducted research activities are subject to these guidelines; thus, any student-conducted research activity that meets the definition of research with human subjects must be reviewed and approved prior to

initiation. This includes class projects, master's theses, doctoral dissertations, and any other project involving human subjects and from which findings may be published or otherwise disseminated.

B. Certain Activities Not Requiring IRB Review

Some research activities do not require prior approval from the Institutional Review Board. The following list is representative but not exhaustive.

1. Emergency Use of Investigational Drug or Test Article

This situation is highly unlikely to arise, given the typical human studies conducted by Georgia Tech faculty. The only activity involving human subjects that is exempt from prior review and approval from the Georgia Tech IRB involves the emergency use of an investigational drug or device (i.e., not approved by the Food and Drug Administration). Emergency use is defined as the use of a test article on a human subject in a life-threatening or severely debilitating situation in which there is no standard acceptable treatment available and in which there is not sufficient time to obtain Georgia Tech IRB approval. Life-threatening and severely debilitating situations also include those wherein irreversible damage (such as permanent brain damage, or loss of sight or limb) may result without the proposed intervention.

The emergency use must be reported to the Georgia Tech IRB within five working days and should include patient history, justification for the emergency use, department chair endorsement, consent form (see subsection a, below), and the investigational drug brochure and/or protocol (generally available from the pharmaceutical company).

Any subsequent use of the investigational drug (i.e., use in another patient) must be approved by the Georgia Tech IRB via the standard application process prior to commencement of the activity.

All investigators should note that *currently published* FDA Guidance can supersede or supplement these Policies and Procedures.

a. Consent Required for Emergency Use

The investigator is required to obtain informed consent of the subject or the legally authorized representative, unless both the investigator and another independent physician certify in writing *all four* of the following:

- the human subject is confronted by a life-threatening or severely debilitating situation necessitating the use of the test article;
- informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent form the subject;
- time is not sufficient to obtain consent from the subject's legal representative, AND
- no alternative method of approved of generally recognized therapy is available that provides an equal or greater likelihood of saving the life of the subject.

If time is not sufficient to obtain an independent physician's determination that the above four conditions apply, the investigator shall make the determination and, within five working days after the use of the drug, have the determination reviewed and evaluated in writing by such a physician. Notification to the Georgia Tech IRB is still required within the five working days.

2. Applications and Proposals Lacking Complete Research Plans

Per §45CFR46.118, applications and proposals lacking complete plans for involvement of human subjects will not require IRB review at the time that the funding proposal is submitted to the potential sponsor. Certain types of applications for grants, cooperative agreements, or contracts are submitted to departments or agencies with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal. These include activities such as institutional type grants when selection of specific projects is the institution's responsibility; research training grants in which the activities involving subjects remain to be selected; and projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. These applications with incomplete plans need not be reviewed by an IRB before an award may be made. However, except for research exempted or waived under §45CFR46.104(d) or §45CFR46.101(i), no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB, as provided in this policy, and certification submitted, by the institution, to the Department or Agency.

3. Quality Assurance and Control, Program Evaluation and Improvement, and Fiscal Auditing

Activities that constitute quality assurance or control, program evaluation or improvement, and fiscal auditing generally do not meet the definition of research. These include activities that are typically not generalizable, such as course evaluations that cannot be generalized to others, and quality assurance activities intended to improve the performance of a unit, division, or department.

C. De-identified Data and De-identified Specimen Analysis Research

Depending on the specifics of the study, Georgia Tech may or may not be engaged in human subjects research when conducting de-identified data and specimen analysis. If the Georgia Tech study team is receiving de-identified data and/or de-identified specimen, and the Georgia Tech study team has no way to re-identify the data and/or specimen, then Georgia Tech is not engaged in human subjects research. Thus IRB review and approval is not required. However, if the Georgia Tech study team is providing a product to be studied at the external institution who is providing the data and/or specimen, then Georgia Tech is engaged in research and IRB review and approval is needed prior to the study taking place.

De-identified Data and De-identified Specimen Analysis		
When GT products are NOT being provided to a third-party		
Can the data and/or specimen be re-identified by GT researchers?	Is a Georgia Tech device* being supplied to third party who is providing GT with data and/or specimen?**	What Type IRB Review?
No	No	None
Yes	No	Exempt, Expedited, or Full***
When GT products are being provided to a third-party		
Can the data and/or specimen be re-identified by GT researchers?	Is a Georgia Tech device* being supplied to third party who is providing GT with data and/or specimen?**	What Type IRB Review?
No	Yes	Exempt or Expedited***
Yes	Yes	Exempt, Expedited, or Full***

**For the purposes of this policy, a "device" is defined as any product, technology, or algorithm developed at Georgia Tech.*
***Is the Georgia Tech study team providing the device to the third-party, who will then conduct a study on the device and send Georgia Tech the results?*
****Dependent on the specifics of the protocol.*

D. Requirement for IRB Review Dependent on Whether Georgia Tech is Engaged in the Research

When Georgia Tech is engaged in the human subjects research activities, the Georgia Tech IRB must review the proposed work.

1. Institutions Engaged in Human Subjects Research

The Office for Human Research Protections (OHRP) considers an institution *engaged* in a non-exempt human subjects research project when its employees or agents for the purposes of the research project obtain:

- data about the subjects of the research through intervention or interaction with them;
- identifiable private information about the subjects of the research; or
- the informed consent of human subjects for the research.

Examples of activities that render the institution *engaged in the research* are:

- Institutions that receive an award through a grant, contract, or cooperative agreement for the non-exempt human subjects research (i.e. awardee institutions), even where all activities involving human subjects are carried out by employees or agents of another institution.
- Institutions whose employees or agents intervene for research purposes with any human subjects of the research by performing invasive or noninvasive procedures. Examples of invasive or noninvasive procedures include drawing blood; collecting buccal mucosa cells using a cotton swab; administering individual or group counseling or psychotherapy; administering drugs or other treatments; surgically implanting medical devices; utilizing physical sensors; and utilizing other measurement procedures.
- Institutions whose employees or agents intervene for research purposes with any human subject of the research by manipulating the environment. Examples of manipulating the environment include controlling environmental light, sound, or temperature; presenting sensory stimuli; and orchestrating environmental events or social interactions.
- Institutions whose employees or agents interact for research purposes with any human subject of the research. Examples of interacting include engaging in protocol dictated communication or interpersonal contact; asking someone to provide a specimen by voiding or spitting into a specimen container; and conducting research interviews or administering questionnaires.
- Institutions whose employees or agents obtain the informed consent of human subjects for the research.

- Institutions whose employees or agents obtain for research purposes identifiable private information or identifiable biological specimens from any source for the research. It is important to note that, in general, institutions whose employees or agents obtain identifiable private information or identifiable specimens for non-exempt human subjects research are considered engaged in the research, even if the institution's employees or agents do not directly interact or intervene with human subjects. In general, obtaining identifiable private information or identifiable specimens includes, but is not limited to:
    - observing or recording private behavior;
    - using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided by another institution; and
    - using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the investigators.

  In general, OHRP considers private information or biospecimen to be individually identifiable as defined in §45CFR46.102(e) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

2. Institutions Not Engaged in Human Subjects Research

It is possible for an entity *not to be engaged* in research, even if the research takes place on its premises. If the Georgia Tech IRB makes a determination that the institution is not engaged, the IRB will not usually review the proposed work.

The following examples of activities that would *not* render Georgia Tech engaged are for illustration purposes; contact the Office of Research Integrity Assurance for a determination of engagement.

- Institutions whose employees or agents perform commercial or other services for investigators provided that **all** of the following conditions also are met:
    - the services performed do not merit professional recognition or publication privileges;
    - the services performed are typically performed by those institutions for non-research purposes; and
    - the institution's employees or agents do not administer any study intervention being tested or evaluated under the protocol.
- Institutions not selected as a research site whose employees or agents provide clinical trial-related medical services that are

dictated by the protocol and would typically be performed as part of routine clinical monitoring and/or follow-up of subjects enrolled at a study site by clinical trial investigators (e.g., medical history, physical examination, assessment of adverse events, blood test, chest X-ray, or CT scan) provided that all of the following conditions also are met:

- the institution's employees or agents do not administer the study interventions being tested or evaluated under the protocol;
- the clinical trial-related medical services are typically provided by the institution for clinical purposes;
- the institution's employees or agents do not enroll subjects or obtain the informed consent of any subject for participation in the research; and
- when appropriate, investigators from an institution engaged in the research retain responsibility for:
    - overseeing protocol-related activities; and
    - ensuring appropriate arrangements are made for reporting protocol-related data to investigators at an engaged institution, including the reporting of safety monitoring data and adverse events as required under the IRB-approved protocol.

Note that institutions (including private practices) not initially selected as research sites whose employees or agents administer the interventions being tested or evaluated in the study—such as administering either of two chemotherapy regimens as part of an oncology clinical trial evaluating the safety and effectiveness of the two regimens—generally would be engaged in human subjects research.

- Institutions (including private practices) not initially selected as a research site whose employees or agents administer the study interventions being tested or evaluated under the protocol limited to a one-time or short-term basis (e.g., an oncologist at the institution administers chemotherapy to a research subject as part of a clinical trial because the subject unexpectedly goes out of town, or is unexpectedly hospitalized), provided that all of the following conditions also are met:
    - an investigator from an institution engaged in the research determines that it would be in the subject's best interest to receive the study interventions being tested or evaluated under the protocol;
    - the institution's employees or agents do not enroll subjects or obtain the informed consent of any subject for participation in the research;

        - investigators from the institution engaged in the research retain responsibility for:
            - overseeing protocol-related activities;
            - ensuring the study interventions are administered in accordance with the IRB-approved protocol; and
            - ensuring appropriate arrangements are made for reporting protocol-related data to investigators at the engaged institution, including the reporting of safety monitoring data and adverse events as required under the IRB-approved protocol; and
            - an IRB designated on the engaged institution's FWA is informed that study interventions being tested or evaluated under the protocol have been administered at an institution not selected as a research site.

- Institutions whose employees or agents:
    - inform prospective subjects about the availability of the research;
    - provide prospective subjects with information about the research (which may include a copy of the relevant informed consent document and other IRB approved materials) but do not obtain subjects' consent for the research or act as representatives of the investigators;
    - provide prospective subjects with information about contacting investigators for information or enrollment; and/or
    - seek or obtain the prospective subjects' permission for investigators to contact them.

An example of this would be a clinician who provides patients with literature about a research study at another institution, including a copy of the informed consent document, and obtains permission from the patient to provide the patient's name and telephone number to investigators.

- Institutions (e.g., schools, nursing homes, businesses) that permit use of their facilities for intervention or interaction with subjects by investigators from another institution.

Examples would be a school that permits investigators from another institution to conduct or distribute a research survey in the classroom; or a business that permits investigators from another institution to recruit research subjects or to draw a blood sample at the work site for research purposes.

- (6) Institutions whose employees or agents release to investigators at another institution identifiable private information or identifiable biological specimens pertaining to the subjects of the research.

Note that in some cases the institution releasing identifiable private information or identifiable biological specimens may have institutional requirements that would need to be satisfied before the information or specimens may be released, and/or may need to comply with other applicable regulations or laws. In addition, if the identifiable private information or identifiable biological specimens to be released were collected for another research study covered by §45CFR46, then the institution releasing such information or specimens should:

- ensure that the release would not violate the informed consent provided by the subjects to whom the information or biological specimens pertain (under §45CFR46.116), or
- if informed consent was waived by the IRB, ensure that the release would be consistent with the IRB's determinations that permitted a waiver of informed consent under §45CFR46.116(e) or (f).

Examples of institutions that might release identifiable private information or identifiable biological specimens to investigators at another institution include:

(a) schools that release identifiable student test scores;
(b) an HHS agency that releases identifiable records about its beneficiaries; and
(c) medical centers that release identifiable human biological specimens.

Note that, in general, the institutions whose employees or agents obtain the identifiable private information or identifiable biological specimens from the releasing institution would be engaged in human subjects research.

- (7) Institutions whose employees or agents:
  - obtain coded private information or human biological specimens from another institution involved in the research that retains a link to individually identifying information (such as name or social security number); and
  - are unable to readily ascertain the identity of the subjects to whom the coded information or specimens pertain because, for example:
    - *the institution's employees or agents and the holder of the key enter into an agreement prohibiting the release of the key to the those employees or agents under any circumstances;*

- *the releasing institution has IRB-approved written policies and operating procedures applicable to the research project that prohibit the release of the key to the institution's employees or agents under any circumstances; or*
- *there are other legal requirements prohibiting the release of the key to the institution's employees or agents.*

For purposes of this discussion, coded means that identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, and/or combination thereof (i.e., the code); and a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

- Institutions whose employees or agents access or utilize individually identifiable private information only while visiting an institution that is engaged in the research, provided their research activities are overseen by the IRB of the institution that is engaged in the research.

- Institutions whose employees or agents access or review identifiable private information for purposes of study auditing (e.g. a government agency or private company will have access to individually identifiable study data for auditing purposes).

- Institutions whose employees or agents receive identifiable private information for purposes of satisfying U.S. Food and Drug Administration reporting requirements.

- Institutions whose employees or agents author a paper, journal article, or presentation describing a human subjects research study.

It is important that the Institutional Review Board concurs with the engagement determination. Contact the Office of Research Integrity Assurance for guidance.

IX. Procedures for Obtaining Institutional Review Board Approval

Revised: July 2024

Research activities that involve the participation of human subjects must be filed with the Office of Research Integrity Assurance for IRB review prior to initiation of the activity. The following steps are required to seek IRB review and approval.

A. Training in Human Subjects Protection: The CITI Modules

As mandated by Georgia Tech's Federalwide Assurance, training in the protections of human subjects is required for all researchers, faculty, staff, students and/or administrators conducting any human subjects research, regardless of funding source or status. The Georgia Tech IRB has approved the Collaborative Institutional Training Initiative (CITI) modules for this purpose.

First time users should complete the initial courses; thereafter, users will complete the refresher courses every three years. The Office of Research Integrity Assurance is informed by email when a person associated with Georgia Tech completes certification requirements. Certification is manually recorded in IRBWISE by the Office of Research Integrity Assurance only when the user is named to the research personnel in a protocol/amendment.

1. Additional CITI Modules Required by Department of Defense

The Department of Defense no longer requires additional training for all personnel conducting or reviewing research involving the Department of Defense. Rather, the Department of Defense accepts the Georgia Tech required CITI modules that are discussed in this section. Please see Appendix 15 for details.

2. Additional CITI Modules for Research with Protected Health Information

If you will access Protected Health Information (PHI), which includes medical records, you will need to complete the "CITI Health Information

Privacy & Security (HIPS)" training in addition to any other required CITI training.

3. Additional CITI Modules for FDA Regulated Research and Clinical Trials

If you are conducting a clinical trial as defined by the FDA, OHRP, or NIH, and/or conducting research on a medical device, drug, biologic, or an in vitro diagnostic involving human subjects or human subjects specimen(s), you will also need to complete the CITI course for "Good Clinical Practice (GCP)." If your study is an NIH funded socio-behavioral clinical trial, then you will need to complete the CITI course for "GCP – Social and Behavioral Research Best Practices for Clinical Research."

4. Training Requirement for Off-Campus Researchers

Off-campus researchers who completed CITI modules through another entity may forward their certificates to the Georgia Tech Office of Research Integrity Assurance.

5. Expired Training

The Office of Research Integrity Assurance will verify currency of training status not only at the time of initial IRB protocol review, but also at the time of review for continuing protocol approval and whenever an amendment or other action is submitted for IRB review. During such review, Research Integrity Assurance will send a reminder to research team members whose training is not current (or is expiring within 30 days), and ORIA will withhold approval until the training requirement is satisfied.

B. Protocol Application

NOTE: The following general information is applicable to all studies. If protocols involve a medical device or study drug, please consult the additional guidance in section XXI of these policies: *"Research Involving Medical Devices or Investigational New Drugs."* If protocols fall under the Limited IRB Review Exempt Categories, please see part 11 of this section.

1. Study Description and Methodology

Protocols must include a study description that states the purpose of the study, including specific objectives and scientific significance. The research methodology must be provided and should define the study population, any instrumentation to be used, and data analysis plans to address the research question. A lay summary is also required and

should be written so that a person unfamiliar with the research can grasp the concepts.

Study types may include observational; record reviews and historical studies; surveys, questionnaires, and interviews; ethnographic studies; case-control studies; prospective studies; and epidemiologic studies or clinical trials.

2. Participant Inclusion, Exclusion Criteria and Justification

Defining the appropriate group of subjects for a research project involves a variety of factors such as the requirements of scientific design, susceptibility to risk, likelihood of benefit, practicability, and considerations of fairness. Note that the IRB is required to make a specific determination that the selection of subjects is equitable.

Inclusion and exclusion criteria for participation must be specified. The investigator must disclose if the investigator or members of the investigator's family as participants. The inclusion of women and members of minority groups and their subpopulations must be addressed in developing a research design appropriate to the scientific objectives of the study. The research plan should describe the composition of the proposed study population in terms of gender and racial/ethnic group, and provide a rationale for selection for such subjects. The exclusion of women must be scientifically justified. The exclusion of children must be scientifically justified in studies where their inclusion is otherwise appropriate.

For clinical protocols, it is important to scientifically justify the number of participants needed and to state a precise number to be enrolled. For non-clinical and minimal risk studies, participant numbers may be stated as a range, (i.e.: *"100-500. We will mail surveys to 500 addresses and hope to have responses from 100 participants*"). If responses are received from more than 100 participants, over-enrollment will not have occurred. Similarly, web-enabled recruitment may result in far more responses than anticipated or needed. If the number of participants has been stated as a range ("*Up to 1000*"), over-enrollment is less likely. Investigators should be prepared to shut down a web recruitment site immediately if responses exceed the number of approved participants. Over-enrollment must be reported to the IRB as a protocol violation or deviation, and it may be unethical to accept responses from participants whose data are not needed and will not be utilized.

3. Recruitment

Participant recruitment procedures should be described, and copies of all advertisements, posters, and verbal scripts must be submitted for review. The word *RESEARCH* should be prominent in the notice. Who will be recruited and how? By recruitment ads, word of mouth, email? If by word of mouth, provide a brief script. The IRB does not expect the script to be followed verbatim; however, the recruitment language must be reviewed. If using flyers, email, advertisements, screen shots from websites, or other documents, submit copies with this protocol.

4. Compensation for Research Participation

Plans for compensating participants must be described in the protocol and disclosed in a separate section of the consent form. See *"Under What Circumstances Can Class Credit Be Given to Student Participants;" "Research Involving Georgia Tech Employees (or Consultants) as Participants;"* and *"Compensation and Incentives for Research Participation*" in these *Policies & Procedures*.

5. Benefits and Risks

Potential benefits, if any, to participants must be stated. If participants are not expected to benefit from being in the study, which is often the case in social and behavioral research, the possible eventual benefits of the research to society should be described. *Compensation is not a benefit of participating in the study.*

Likewise, any known or anticipated potential discomforts or risks (probability of harm) to participants must be disclosed in the consent process and documents. Risks may be physical, psychological, social, and economic. In social and behavioral research, disclosure of personal information is usually the greatest risk to participants (i.e., where such identification of the subject and/or his responses could place the participant at risk of criminal or civil liability, or could be damaging to the participant's financial standing, employability, or reputation). The Research Associate should be contacted for information concerning Certificates of Confidentiality if a principal risk of the study is harm caused by loss of confidentiality

If a protocol poses minimal risk, some version of the following statement is appropriate for use in the consent documents:
"*The probability and magnitude of harm or discomfort anticipated in the proposed research are not greater than those ordinarily encountered in everyday life or during performance of routine physical or psychological examinations or tests.*" If the reading level needs to be lowered for the subject pool, this statement might be rephrased as follows: "*The chances*

of your being hurt or upset by this study are about the same as with your regular everyday activities or with taking physical or psychological exams or tests."

6. Special Protections for Vulnerable Participants

The federal regulations provide for special protections for vulnerable groups, defined in the regulations as fetuses, minors, those who are unable to consent for themselves, prisoners, economically or educationally disadvantaged persons and, in some cases, pregnant women. In some cases, research involving students may render them vulnerable. If members of vulnerable groups are to be enrolled, the additional protections that will be put into place must be specified to ensure that the rights and welfare of such groups are protected. See guidance at Section XI., "Research Involving Vulnerable Populations: Children, Prisoners, Pregnant Women and Fetuses" in these *Policies & Procedures*.

7. Consent, Parental Permission, and Assent Forms

(See "*Informed Consent*" in these *Policies & Procedures* for a more complete discussion of consent. Also consult section *XXVI.B.7.* for a full discussion of records retention requirements, i.e., consent forms must be kept by the investigator in an accessible format for three years after the study closes).

Note that *consent forms* are used when enrolling participants 18 years or older, *assent forms* are used when enrolling minors, defined in the Georgia Statutes as those persons under age 18; and *parental permission forms* are used to obtain permission from parents of participants 17 years or younger (since minors cannot consent to being in the study).

All studies that offer monetary compensation must state the following in the Compensation section of the consent form: "U.S. Tax Law requires that a 1099-misc be issued if U.S. tax residents receive $600 or more per calendar year. If non-U.S. tax residents receive more than $75, mandatory 30% withholding is required. Your address and Tax I.D. may be collected for compensation purposes only. This information will be shared only with the Georgia Tech department that issues compensation, if any, for your participation."

a. Consent Templates

Consent and assent forms and parental permission forms should generally conform to the Georgia Tech format. Consent and assent form templates and a parental permission template are posted to

the Office of Research Integrity Assurance website. See the section on *Informed Consent* of these *Policies & Procedures* for further guidance.

b. Consent for Non-English Speaking Participants

Another important aspect of the consent process is to provide the information in a language understandable to the subjects. See also *"Research in International Settings," "Obtaining and Documenting Informed Consent of Subjects Who Do Not Speak English"* and Appendix 7, *"Sample Short Form Written Consent Document for Subjects Who Do not Speak English"* of these *Policies & Procedures* for a complete discussion of methods for obtaining consent from non-English speaking subjects.

- Written consent: For those consent forms that must be translated into (or from) a foreign language, the protocol must contain a certified affidavit of accurate translation from an appropriate translator who is unaffiliated with the study. The translated consent form and affidavit must be submitted and approved by the IRB before use of the consent form. Alternatively, departments must provide a charge number so that the Office of Research Integrity Assurance may obtain the certified translations. (NOTE: If the project is not funded, contact the Office of Research Integrity Assurance for assistance with funding translations).
- Oral presentation of informed consent information in conjunction with a short form written consent document: The second method involves use of an IRB-approved English language consent form, an IRB-approved short consent form written in the non-English language, and a witness fluent in both English and the language of the subject. A sample short form is provided in Appendix 7 to these *Policies & Procedures*. See also "Informed Consent" within these *Policies & Procedures*. The consent form(s) must be submitted to the IRB in English and in the participants' native language.
- While research subjects should be compensated for their time and trouble, it is important to remember that *such compensation does not constitute wages for services performed*. There is no employer/employee relationship between a researcher and a research subject. Nevertheless, US tax law imposes a mandatory withholding of 30% for nonresident alien payments; therefore, all payments made to nonresident aliens must be processed by Accounts Payable, regardless of the amount.

8. Data Storage and Confidentiality

The data storage and confidentiality section of the protocol should describe the extent to which confidentiality of records identifying the participant will be maintained. If the study involves use of video- or audio-taping of participants, specifically address who has access to the tapes, how tapes are stored, for what purposes they will be used, and what happens to the tapes once the study ends. Disclose whether tapes are erased after all the necessary information is collected from them and whether tapes are kept for archival purposes

If data will be stored in a repository, see section XVI, "Repositories, Tissue Banks, Biobanks; Registries and Data Banks; and Databases." Also see the Appendices to these *Policies & Procedures* for a more complete discussion of data storage topics. Also see the Office of Information Technology guidance on *Protecting Sensitive Data in Electronic Format* and *Best Practices for Backing Up Sensitive Data*. The Georgia Tech Library also provides data management plan guidance at https://policylibrary.gatech.edu/research/protecting-sensitive-data.

9. Grant or Sponsor Proposal

When funding is being sought from an external sponsor, whether federal or industry, the funding proposal must be attached. If the protocol is not funded, the related thesis, dissertation or seed grant description, if any, should be attached. This is in addition to, not in lieu of, the project description described herein.

10. Additional Materials to Be Submitted for Review

Interview guides, surveys, standardized tests, and questionnaires must be reviewed along with all other elements of the proposed study. If a medical device will be utilized, the manufacturer's brochure must be provided. Clinical studies must include an Investigator's Agreement; see *Investigator Agreement* at Appendix 17.

a. Documentation of Authorization to Collect Data at Non-Georgia Tech Site

If the Georgia Tech investigator will collect data or conduct other research activities at sites other than Georgia Tech, the investigator must submit documentation of authorization from each site.

11. Exempt Review Submission Process

To request for Exempt Review Determination, the PI must submit to the IRB in IRB Wise. When submitting, the PI will need to complete Section I. "General Information," Section II. "Research Design and Methodology" question, J-N (only if funded), Section III. "Subject Information, Consent and Types of Studies" question E (only if you are obtaining an identifiable dataset or identifiable human specimen), Section IV. "Studies involving Department of Defense, Radiation, or Nanotechnology," upload all of the study documents to Section VI. "Attach Documents," and complete the "Conflict of Interest" section. More information may be requested and additional sections within IRB Wise may need to be completed due to the specifics of the study.

Please note that all documents, including but not limited to consent, recruitment, funding proposals, data collection instruments (e.g., surveys, interview guides, etc.) are required to be uploaded in the submission. Lastly, all other requirements that may apply to the study (e.g., required training, PI eligibility, etc.) still apply to the Exempt research.

C. Protocol Signoffs

Several signoffs are required before the IRB will review a protocol.

1. Faculty Member as Principal Investigator

The faculty member serving as Principal Investigator electronically signs off on the protocol, documenting the accuracy of the submitted materials and certifying the lack of a conflict of interest (or disclosing it), and that, upon IRB approval, will ensure compliance with the IRB policy, "Investigator's Responsibilities When Conducting Research Activities Subject to DHHS or FDA Regulations," presented in these *Policies & Procedures*.

a. Dissertation or Thesis Research Conducted by Student
Students may generally not be Principal Investigators on protocols. When a student is conducting research for their dissertation or thesis, the academic advisor should be named Principal Investigator and the student takes the role of co-investigator. The faculty member's signature documents that the faculty member has read the student's protocol and assumes responsibility for all aspects of the study including recruitment, informed consent, data collection, storage and confidentiality of data, and participant safety.

2. Departmental Signoff

The electronic signature of the department head (or designee) indicates that the protocol is appropriate to be conducted in the department, that the PI has adequate expertise in the subject matter and in research, that the research staffing is appropriate, and that the chair/designee agrees that the research can and should be conducted within their department.

3. Department Chair as Principal Investigator

When the Principal Investigator is also the Department Chair, there is no additional signoff required. The Chair may submit the protocol directly to the Institutional Review Board.

4. Vehicular Transportation of Research Subjects by Georgia Tech Personnel

Occasionally, investigators may need to transport human subjects by vehicle. *An approved transportation service provider is available via BuzzMart.*

If it is proposed that a Georgia Tech employee will drive a vehicle to transport human subjects, the Institutional Review Board must ensure that Institute policy (*Office of Insurance, Claims & Property Control/Business Services*), excerpted and bulleted below, is followed.

- The transport by an employee of persons in a vehicle must be specified in the employee's official job duties.
- The employee must pass a Motor Vehicle Report (driving history), which must be ordered through the Office of Human Resources.
- The employee must complete the Defensive Driving class through Environmental Health & Safety (EHS).
- If the employee will be operating a van, he/she must also complete the Van Safety class through EHS.
- It is recommended that employees operate an Institute vehicle to transport human research participants, instead of their personal vehicles, in order to avoid personal auto insurance coverage complications. GT employees should not direct anyone to use a personal vehicle to transport GT research participants.
- If investigators plan to arrange for research participants to use taxi or commercial driving services, the driving service vendor should be under contract, and subject to GT insurance requirements, including a minimum business auto liability insurance limit of

$3,000,000 per occurrence, including naming GT (BOR) as an additional insured.

- Research participants shall not be transported by students who are not Graduate Research Assistants (GRAs) and, therefore also not employees.
- Documentation of satisfactory completion of these requirements must be included in the IRB protocol.

X. Informed Consent

Revised: July 2024

The principle of respect for persons, as set forth in the *Belmont Report*, states that the consent process must address three elements: *information, comprehension and voluntariness*. Sufficient and complete information about the study must be provided in language comprehensible to the participant. The investigator must clearly convey to participants what they are agreeing to do and ensure that they understand (comprehend). Participants' agreement must be given voluntarily (freely) and without undue influence. This communication occurs in the consent process and is generally documented in the written consent form.

A participant may generally not be enrolled in research unless the investigator has obtained his informed consent or that of the participant's legally authorized representative. See *X. Informed Consent, C. Exception to the Requirement for Documenting Informed Consent 1., 2., and 3.* for a discussion of consent waivers and studies involving deception or concealment.

The process of obtaining and documenting informed consent must comply with the requirements of DHHS regulations at §45CFR46.116 and §45CFR46.117 and the FDA consent requirements provided in §21CFR50.20-27 and §21CFR56.109. The IRB may impose additional requirements that are not specifically listed in the regulations to ensure that adequate information is presented in accordance with institutional policy and local law.

A. Elements of Consent

The federal regulations require that certain information must be provided to each subject

1. For all Expedited and Full Board research, the regulations state that the Consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

2. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;

- Consent forms must disclose that participants are being asked to be a volunteer in a *research* study. Protocols that pose greater than minimal risk to participants, such as experimental medical treatments, must include language substantively similar to the following two sentences: *"You are encouraged to take your time in making your decision. Discuss this study with your friends and family."*
- This section must include a description of all research procedures; the frequency, scheduling and time commitment of each procedure and visit; and the total time commitment. Any audio or videorecording should be addressed in this section as well. If participants are being randomly assigned to different groups, this should be disclosed with a statement such as "You will be randomly (by chance, like flipping a coin) assigned to one of…." Investigators should ask potential participants short questions after the research has been described and the consent form read, in order to assess that the potential participant has at least a basic understanding of what the research involves. For example: *"Tell me in your own words what this study is all about." "What do you think will happen to you in this study?" "What do you expect to gain by being in this study?" "What risks might you experience?" "What options do you have if you decide you don't want to be in this study?"*

3. A description of any reasonably foreseeable risks or discomforts to the subject;

- *Any known or anticipated research-related injury (i.e. physical, psychological, social, financial, or otherwise) must be disclosed during the consent process and described in the consent documents. In research that is more than minimal risk, an explanation must be given regarding whatever voluntary compensation and treatment will be provided in the event of injury, harm, or discomfort. Note that the regulations do not limit injury to physical injury, which is a common misinterpretation.*

4. A description of any benefits to the subject or to others which may reasonably be expected from the research;

- *Describe the benefits that subjects may reasonably anticipate. If none are anticipated, it is appropriate to say so and to indicate the benefits that may eventually accrue to society.*

5. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

- *This section generally appears in consent documents for clinical studies. If any exist, describe the alternatives to participating in the research project. For example, in drug studies the medication(s) may be available through the family doctor or clinic without the need to volunteer for the research activity. If participants are already receiving medical treatment for the study condition, they should be told whether continued routine treatment is a suitable alternative to participation in the study.*

6. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

- See Appendices of these *Policies & Procedures* for a discussion of Certificates of Confidentiality and for data storage guidance. Also, see guidance from Office of Information Technology at http://www.oria.gatech.edu/.
- *In some studies, the greatest risk to participants is that of inadvertent disclosure of personal information that could reasonably place participants at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation. For other good reasons, researchers also desire to securely store research data.*
- *Will participant responses be separated from their identities? Will there be a key or code that links these? If so, how will these be safeguarded?*
- *If the study involves use of audio or video recording of participants, specifically address who has access to the recordings, how the recordings are stored, for what purposes they will be used, and what happens to the recordings once the study ends. State whether recordings are erased after all the necessary information is collected from them and whether tapes are kept for archival purposes.*
- *Web-based research has its own special set of privacy concerns. State whether the server to be used is a secure https server of the kind typically used to handle credit card transactions. What information will be stored on the server, for how long, and who has access to it?*
- *See Office of Information Technology guidance on Protecting Sensitive Data in Electronic Format and Best Practices for Backing Up Sensitive Data at* https://policylibrary.gatech.edu/research/protecting-sensitive-data.
- *Some studies inherently are in need of a Certificate of Confidentiality which protects the investigator from involuntary release (e.g., subpoena) of the names or other identifying*

characteristics of research subjects. The IRB will determine the level of adequate requirements for confidentiality in light of its mandate to ensure minimization of risk and determination that the residual risks warrant involvement of subjects.

7. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

8. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject;

- *The regulations provide for the identification of contact persons to answer participants' questions about the research, their rights as a research subject, and research-related injuries. These three areas must be explicitly stated and addressed in the consent process and documentation. Furthermore, a single person is not likely to be appropriate to answer questions in all areas because of potential conflicts of interest or the appearance of such. Questions about the research or research-related injuries (where applicable) are frequently best answered by the investigator(s). Questions about the rights of research subjects should be addressed by the Office of Research Integrity Assurance. Therefore, each consent document must have at least two contact names with local telephone numbers and email addresses to answer questions in these specified areas.*

9. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. The statement regarding voluntary participation and the right to withdraw at any time can be taken almost verbatim from the regulations (§45CFR46.116(b)(8)).

The regulations further provide that the following additional information be provided to subjects, where appropriate:

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
3. Any additional costs to the subject that may result from participation in the research;

4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
5. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject;
6. The approximate number of subjects involved in the study;
7. Inclusion and exclusion criteria for studies that, based on a scientific justification, are limited to certain categories of participants;
8. Compensation scheme. This section of the consent form should specify participant compensation and reimbursement, whether monetary, gift card, or class credit. Compensation should be prorated in cases where participants may make several trips or go through a number of sessions. It is generally inappropriate to pay bonuses for completion or to withhold payment until the study is completed. Disclose whether compensation will be prorated to those who withdraw early or do not complete the study. If there is no compensation at all, this should be disclosed. The IRB recommends that full compensation be given when participants must stop due to a physical inability to complete the study. See "Research Involving Georgia Tech Students as Participants;" "Research Involving Georgia Tech Employees (or Consultants) as Participants;" and "Compensation and Incentives for Research Participation" in these *Policies & Procedures*.
9. Disclosure of Conflict of Interest is required if the Principal Investigator or anyone else on the research team has a conflict of interest in this study. It is not inherently unethical to have a conflict of interest; it is, however, prudent—and required—that it be disclosed to potential participants and be suitably managed. Such conflicts must be disclosed to the faculty member's department, and a management plan must be on file with the Conflict of Interest team at Georgia Tech. Contact the Office of Research Integrity Assurance for guidance.
10. Language and readability must be appropriate for the subjects. Think of the consent document as a teaching tool, not as a legal instrument. It is not a contract between participant and researcher! The consent document should be written in second person; i.e., *"If you agree to be in this study, you will be asked to…"* Use of the first person (e.g., *"I understand that …"*) can be interpreted as suggestive, may be relied upon as a substitute for sufficient factual information, and can constitute coercive influence over a subject. Use of scientific jargon and legalese is not appropriate.

    Note that the average person reads at the 8th grade level, and consent forms intended for that population should be written at that reading

level. Investigators are encouraged to use computer software applications or other techniques to assess reading level of the finished document; use a large font; use short, simple sentences, and avoid technical language; define all abbreviations and acronyms when they first appear in text. Before submitting a consent form for IRB review, the reading level should be checked. One resource for checking reading level is in Microsoft Word; the Flesch-Kincaid Grade Reading Level can be found under the Tools menu, Spelling and Grammar section, under Options.

B. Resources for Developing a Consent Process

1. Templates

Researchers must utilize only the currently approved, IRB-stamped version of consent, permission and assent documents in the consent process with subjects. These documents must be amended, with the Georgia Tech IRB approval, if and when new information becomes available, due to either protocol amendment or the discovery of new adverse events that may be associated with participation. Once amended and Georgia Tech IRB-approved, only these most current versions may be used to consent new subjects. The older versions of these documents are voided and must not be used again in the consent process. A consent addendum should be used to provide the new information to the subjects already enrolled in the study.

Consent document samples containing the required elements of consent and the additional language required by the Georgia Tech IRB are posted at https://oria.gatech.edu/irb/submitting-protocol/forms.

C. Exception to the Requirement for Documenting Informed Consent

DHHS provides for waiving or altering elements of informed consent under certain conditions. FDA has no such provision because the types of studies that would qualify for waiver or alteration are either not regulated by FDA or are covered by the emergency treatment provisions of §21CFR50.23. Where a protocol is subject to review under more than one department or agency's regulations, the requirements of each set of regulations must be met.

1. Waiver of Documentation of Informed Consent:

In certain circumstances (use of an anonymous survey, a telephone survey, or a web-based survey), investigators may seek a waiver from the requirement to document informed consent. That is, *they intend to obtain informed consent, but there will be no written document signed by the participants.*

The Georgia Tech IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if the IRB determines that:

> (i) That the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern;
>
> (ii) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; or
>
> (iii) If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

In cases where the requirement of documentation is waived, a consent document in IRB-recommended format should still be used. However, the document is written in letter format ('Dear Subject') and, rather than requiring the subject's signature to verify consent, the following text is used to end the letter:

"If you _____ (e.g., complete the attached survey, answer these few questions etc.), it means that you have read (or have had read to you) the information contained in this letter and would like to be a volunteer in this research study. Thank you, (signatures of investigators)"

2. Waiver of Informed Consent

Written informed consent is not always appropriate, especially in the social and behavioral studies. The DHHS regulations at §45CFR46.116(f) establish five criteria for waiving consent or altering the elements of consent in minimal risk studies. *There are no corresponding provisions in FDA regulations, and these criteria may not be used to waive or alter the elements of consent in FDA-regulated studies*:

> (i) The research involves no more than minimal risk to the subjects;
>
> (ii) The research could not practicably be carried out without the requested waiver or alteration;

(iii) If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;

(iv) The waiver or alteration will not adversely affect the rights and welfare of the subjects; and

(v) Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

Most complete waivers of consent involve studies in which there are minimal risks to subjects, but complete waivers are also possible in emergency care and a few other circumstances.

An example of research for which a waiver of informed consent is appropriate is one in which the only involvement of human subjects is that of anonymous observation, as provided in the federal guidance governing exempt studies. The Food and Drug Administration (FDA) permits an exception to the informed consent requirement before the emergency use of a test article, *under certain conditions*.

Studies regulated under the FDA regulations differ from HHS regulations and are generally more restrictive in the area of waiver of informed consent. The differences are noted below.

3. Deception or Concealment in Research

Sometimes, particularly in social/behavioral research, investigators plan to withhold information about the real purpose of the research or even to give subjects false information about some aspect of the research. *Deception* in a study occurs when participants intentionally are told something untrue about the study, such as its real purpose. By its very nature, deception in research violates the principles of voluntary and informed consent to participate in research. Therefore, deception is an extraordinary measure that is not normally permitted in human subjects' research. *Concealment* occurs when the researcher intentionally withholds some of the research details from participants and may elicit somewhat less heightened concern.

a. Consent Criteria When Deception is Used

Deception can only be allowed when a waiver of informed consent is justified in accordance with §45CFR46.116(f). When proposed, the deception must meet all the following criteria:

- Risks to subjects are no greater than minimal.
- The rights and welfare of subjects must not be adversely affected.
- Deception is essential in order for the investigator to carry out the research.
- At the earliest possible time, subjects must be informed of the nature of the deception and be given a reasonable opportunity to withdraw from participation and to have their data excluded.

b. Other Important Issues with Deception Studies

The IRB will expect the following issues to be addressed in protocols involving deception:

- A reasonable person would be willing to participate in the research if the person knew the nature and procedures of the study.
- Any data collected during the deception may be used only with a subject's explicit approval, obtained *after* the subject has received full disclosure regarding the study.
- The proposed research is sound in theory and methodology.
- Anticipated findings will contribute significantly to the general body of knowledge.
- Vulnerable subjects (the cognitively impaired, children, or prisoners) are excluded from research involving deception.

c. Consent Language When Deception or Concealment Will Be Used

When deception will be used during a study, the investigator should either disclose during the consent process that deception or concealment will be used OR justify withholding that information. If investigators will disclose the use of deception or concealment, some version of the following language should appear in the procedures section of the consent documents:

"During the study, you may be led to believe some things that are not true. When the study is over, we will tell you everything. At that time, you may decide whether to allow us to use your information. You have the right to require your information be destroyed."

For studies proposing concealment, the following language is recommended for the procedures section of the consent documents:

"We will not tell you everything about the study in advance. When the study is over, we will tell you everything. At that time, you may decide whether to let us use your information. You have the right to require your information be destroyed."

If deception is proposed in internet research, see "XVII. Research Using the Internet" in these *Policies & Procedures*.

D. Obtaining and Documenting Informed Consent of Subjects Who Do Not Speak English

The Georgia Tech IRB follows the November 9, 1995 guidance issued by the Director, Division of Human Subject Protections, Office for Protection from Research Risks (OPRR), as follows:

Department of Health and Human Services regulations for the protection of human subjects require that informed consent information be presented *in language understandable to the subject* and, in most situations, that informed consent be documented in writing (§45CFR46.116 and §46.117).

1. Written Consent

Where informed consent is documented in accordance with §46.117(b)(1), the written consent document should embody, in language understandable to the subject, all the elements necessary for legally effective informed consent. Subjects who do not speak English should be presented with a consent document written in a language understandable to them. For those consent forms that must be translated into (or from) a foreign language, the protocol must contain a certified affidavit of accurate translation from an appropriate translator who is unaffiliated with the study. The translated consent form and affidavit must be submitted and approved by the IRB before use of the consent form. *See Appendix 23 regarding translation.*

2. Oral Presentation of Consent Information with Short Form

Alternatively, §46.117(b)(2) permits oral presentation of informed consent information in conjunction with a short form written consent document stating that the elements of informed consent required by §46.116 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the

witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form. The IRB must receive all foreign language versions of the short form document as a condition of approval under the provisions of §46.117(b)(2).

- Written consent: For those consent forms that must be translated into (or from) a foreign language, when this procedure is used with subjects *who do not speak English*,
    - the oral presentation and the written short form document should be in a language understandable to the subject;
    - the IRB-approved English language informed consent document may serve as the summary; and
    - the witness should be fluent in both English and the language of the subject.
    - the short form document should be signed by the subject (or the subject's legally authorized representative);
    - the summary (i.e., the English language informed consent document) should be signed by the person obtaining consent as authorized under the protocol; and
    - the short form document and the summary should be signed by the witness. When the person obtaining consent is assisted by a translator, the translator may serve as the witness.

  See the Appendices for a sample short form. Appendix 23 specifies that the protocol must contain a certified affidavit of accurate translation from an appropriate translator who is unaffiliated with the study. The translated consent form and affidavit must be submitted and approved by the IRB before use of the consent form. In some cases, the IRB may require that the documents be translated back into English by another translator, to ensure accuracy and completeness. (NOTE: If the project is not funded, contact the Office of Research Integrity Assurance for assistance with obtaining translations).

E. Consent Language When DEXA Scans Are Being Conducted

The following language was provided by the Georgia Tech Radiation Safety Office, a unit of Environmental Health and Safety (EHS). This language must be included in consent forms for studies involving DEXA scans.

"This research study involves exposure to radiation from a DEXA whole body scan. This radiation exposure is not necessary for your medical care and is for research purposes only. The total amount of radiation that you will receive in this

study is equivalent to a uniform whole-body exposure to 1/2 day of exposure to natural background radiation. This use involves minimal risk and is necessary to obtain the research information desired."

XI. Research Involving Vulnerable Populations: Children, Prisoners, Pregnant Women and Fetuses

Reviewed: July 2024

When some or all of the research participants are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, the Institutional Review Board is required to verify that additional safeguards have been included in the study to protect the rights and welfare of these participants. Federal regulations stipulate that if Institutional Review Boards regularly review research involving a vulnerable category of subjects, consideration should be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects. The Georgia Tech Central IRB is properly constituted to review research involving vulnerable populations.

A. Research Involving Children (Minors)

See Appendix 10 of these Policies & Procedures an update from the National Institutes of Health Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects. As of 2016, NIH refers to those under the age of 18 as children, instead of those under the age of 21.

The State of Georgia defines children, or minors, as those persons under the age of 18.

1. Determination of Risk in Research Involving Children

a. Research of Minimal Risk Involving Children

The IRB will approve research of minimal risk that involves children if it finds that no greater than minimal risk to children is presented and only if adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.

b. Research of Greater Than Minimal Risk Involving Children

The IRB will approve this type of research only if the proposed intervention or procedure holds out the prospect of direct benefit

for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, and only if the IRB finds that:

- the risk is justified by the anticipated benefit to the subjects;
- the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
- adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in §46.408.

c. Research Involving Greater Than Minimal Risk Involving Children and with No Prospect of Direct Benefit to Individual Subjects, but Likely to Yield Generalizable Knowledge about the Subject's Disorder or Condition

- The IRB will only approve such research if it finds that:
- the risk represents a minor increase over minimal risk;
- the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
- the intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
- adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.

d. Research Not Otherwise Approvable which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children

The IRB will approve research that does not meet the requirements of §46.404, §46.405, or §46.406 only if:

- the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and
- the Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either:
    - that the research in fact satisfies the conditions of §46.404, §46.405, or §46.406, as applicable, or the following:

- the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
- the research will be conducted in accordance with sound ethical principles;
- adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in §46.408.

2. Parental or Guardian Permission and Assent

With some exceptions, the Georgia Tech IRB requires that *parental* or *guardian* permission be obtained prior to a minor's participation in a research study, since the minor cannot legally consent to such participation. Depending on the age and maturity of the potential subjects, the Georgia Tech IRB may require that the minor be presented with an assent form to review and sign.

Researchers may not utilize "implied permission," wherein a parent's permission is assumed unless the parent specifically declines in writing. That is, if permission forms are sent home and not returned, the researcher may not assume that parental permission has been granted. The researcher may also not send children home with a parental permission form that says "Send this signed form back if you don't want your child to participate."

Guidance on developing language for parental/guardian permission and for assent can be found in the consent templates at http://oria.gatech.edu/irb/submitting-protocol/forms.

3. Waiver of Parental or Guardian Permission

Per §45CFR46.116(f), an Institutional Review Board may approve a consent procedure which does not include some or all of the elements of informed consent, or the Board may waive the requirements to obtain informed consent provided the IRB finds and documents that:

- the research involves no more than minimal risk to the subjects;
- the waiver or alteration will not adversely affect the rights and welfare of the subjects;
- the research could not practicably be carried out without the waiver or alteration; and
- whenever appropriate, the subjects will be provided with additional pertinent information after participation

4. Research Involving Children Who Are Wards or Juvenile Detainees

In accordance with §45CFR46.409, the Georgia Tech IRB will approve research proposing to enroll children who are wards of the State or any other agency, institution, or entity only under certain conditions. If the research fits into one of the following two categories, it can only be approved if related to their status as wards or conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards:

- Research involving involves greater than minimal risk and no prospect of direct benefit to individual subjects, but is likely to yield generalizable knowledge about the subject's disorder or condition
- Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

In certain circumstances, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

Juvenile detainees constitute an especially vulnerable population. In addition to considerations required by §45CFR46, Subpart C (*Additional DHHS Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects*), the guidance at Subpart D (*Additional DHHS Protections for Children Involved as Subjects in Research*) must be followed.

a. Constructive Emancipation of Minors

In some cases, a minor may be constructively emancipated and be granted by the state the legal authority to consent to participate in research. In these cases, the IRB must carefully weigh the potential subject's vulnerability, developmental age, and the fact that the parents' rights have been subjugated to the state or other agency, institution, or entity. The IRB may, at its discretion, appoint an advocate for these emancipated minors.

5. Categories of Review When Participants Are Minors

All protocols involving minors will fall into one of these categories.

a. Exempt
The exempt review category and corresponding review procedure apply to research involving minor subjects with the exception of exemptions #2(iii) and #3. Research of this type *is not exempt from further review* unless it only involves the observation of public behavior, *and* the investigator does not participate in the activities being observed. Under exemption 1, minor subjects can be enrolled in research conducted in established or commonly accepted educational settings that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods. Under exemption 2 (i) and 2 (ii), minor subjects can be enrolled in research involving educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed.

b. Expedited
The expedited review category and corresponding review procedure are applicable to research involving minor subjects, as long as the particular activity in that section does not require that the subject be 18 years old or older.

c. Full Board
All other research involving minor subjects must be reviewed by the full board.

B. Research Involving Prisoners

The Georgia Tech Central Institutional Review Board is properly constituted to review and approve research involving prisoners as subjects.

A prisoner may be defined as any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statue. Individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing (§45CFR46.303(c)).

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to participate in research activities for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma.

For these purposes, “prisoners” include incarcerated persons convicted of crimes and other persons held against their will, such as detainees awaiting bail or trial. The term is intended to encompass individuals sentenced under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

The federal regulations at *§45CFR46 Subpart C* specifically address research involving prisoners. One stipulation of these regulations is that Institutional Review Boards are required to have a prisoner representative as a member of the IRB when protocols involving prisoners are being reviewed. (Georgia Tech’s Central IRB has a prisoner representative member). Federal regulations specifically preclude protocols involving prisoners from review under the exempt category and from research involving deception.

If a research subject becomes a prisoner while enrolled in a research study, the Investigator must immediately report this in writing to the Office of Research Integrity Assurance. All interactions or interventions with the prisoner-participant must be halted until approval can be obtained from the Georgia Tech IRB and, *if funded by NIH*, the federal Office for Human Research Protections (OHRP). As stated earlier, the Georgia Tech Central IRB is properly constituted to review and approve research involving prisoners.

If the study falls under the Exempt review process, then prisoners can only be included if the research is aimed at involving a broader subject population and the prisoners are only incidentally included. In this case, the review outlined in Subpart C will not occur, as the study is exempt from this process.

C. Research Involving Pregnant Women and Fetuses

In much behavioral research, participant pregnancy may be irrelevant for purposes of the study. For example, the completion of opinion surveys and

questionnaires would hardly be viewed as posing greater than minimal risk to the pregnant woman or fetus. There are additional precautions and requirements, however, that apply when enrolling pregnant women in research, particularly that of a clinical nature.

In accordance with §45CFR46.204, research involving pregnant women or fetuses may be approved if all of the following conditions are met:

- Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
- The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
- Any risk is the least possible for achieving the objectives of the research;
- If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of §45CFR46 Subpart A;
- If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of §45CFR46 Subpart A, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
- Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- For children as defined in §45CFR46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of §45CFR46 Subpart D;
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- Individuals engaged in the research will have no part in determining the viability of a neonate.

1. Pregnancy Testing

Some research studies may present a risk to pregnant women and their fetuses. In order to determine whether a pregnancy test is appropriate for women of childbearing potential who may enroll in a study, the IRB has developed the following guidance.

a. Greater Than Minimal Risk to Fetus with No Benefit to Fetus or Mother

If participation in research involves exposure to a risk factor known to be more than minimal risk to a fetus, with no benefit to the fetus or mother, the investigator has a responsibility to actively screen for pregnancy before enrolling, and if exposure continues, the pregnancy screening must continue. Simply relying on the participant's knowledge or belief about whether she is pregnant is insufficient if better screening methods are available. Pregnancy screening may involve a urine test or blood test, or if these are not practical, it could involve explicit questioning about behavior and medical history, e.g., whether the person is sexually active and using birth control, whether the person has had a medical procedure (or a health condition) that prevents her from being pregnant, etc.

b. No additional Risk to Fetus

If participation in research involves exposure to risk factors that are known to pose no additional risks to a fetus, such as participation in a typical test of cognitive functioning, it is improper to exclude women who are or might be pregnant from the study on that basis.

c. Unknown but Presumed Risk to Fetus

If participation in research involves exposure to risk factors that are of unknown significance to a fetus but might reasonably be expected to be a potential risk because they involve exposure to chemicals, radiation, physical forces, pathogens, etc. that are known to adversely affect human tissue or cell division or nutrition, etc., the investigator (with IRB oversight) must weigh the potential risk against any benefits. If there are no potential benefits to the mother or fetus, these exposures may be treated as category a above until such time as evidence can be obtained to move it into category b. (If there are potential benefits to the mother, these may be considered and weighed against the risk to the mother + possible fetus).

d. Unknown Risk to Fetus

If participation in research involves exposure to risk factors that are generally held to be safe for humans, but effects on fetuses are simply unknown, this must be disclosed to all participants so they

can make an informed decision about whether to participate, but pregnancy or potential pregnancy cannot be used as an exclusion criteria. Consent documents for these cases shall include the following language: *"Women of childbearing potential who are considering being in this study should especially note that the risk to fetuses of exposure to XXXX are currently unknown."*

2. Exempt Research

The exemptions listed under 45 CFR 46.104 may be applied to research subject to subpart B if the conditions of the exemption are met.

XII. Research Involving Georgia Tech Students as Participants

Revised: July 2024

Given the vast amount of research conducted at the Georgia Institute of Technology, it is not surprising that Georgia Tech students are frequent participants in research studies conducted by faculty and other students. Participation in research can be a valuable experience for students to learn about the conduct of scientific research; therefore, the educational benefit of their participation should not be discounted. These guidelines are designed to assist faculty members who wish to enroll Georgia Institute of Technology students as subjects in research protocols. Additionally, when requesting to use student records for research purposes, a formal request must be made to the Registrar's Office. This process is outlined in Part C of this section.

Students are entitled to the same protections and considerations given other research subjects, but some issues are of special concern when students are being recruited for studies conducted by their current faculty. For example, students may have a perception of coercion to participate. There is also some controversy about whether students are entitled to a reasonable expectation of privacy in the classroom and whether behavior in the classroom constitutes public behavior. Video recording in the classroom can present a dilemma for students who do not wish to participate but who also realize that they cannot inconspicuously decline. For these and other reasons, the Georgia Tech IRB includes a student as a full voting member of the Board.

A. Use of Researcher's Students as Subjects

An underlying principle of the regulations governing use of human subjects in research is that the subject's participation is voluntary, based upon full and accurate information. The relationship of teacher and student is inherently one that raises the issue of "voluntariness." No matter how well intentioned the teacher is, students may feel compelled to participate and may believe that failure to do so will negatively affect their grades and the attitude of the teacher (and perhaps other students) toward them. The Georgia Tech IRB recognizes, however, that in some research situations, use of one's students is integral to the research. This is particularly true of research into teaching methods, curricula and other areas related to the scholarship of teaching and learning.

The Georgia Tech IRB has taken the position that faculty should not use their own students as subjects in their non-exempt research if it can be avoided. The following are two models of research design that are recommended by the Georgia Tech IRB for such non-exempt studies.

1. Collection of Data by Third Party

In situations where the activities to be undertaken by the students *are not part of required class activities*, and thus students may choose whether to participate, the instructor/researcher should arrange to have enrollment and consent handled by an independent third party who also collects the data, so that the instructor does not have access to the identifiable data or identity of participants for any purpose until grades have been assigned and posted.

2. Collection of Data by Instructor/Researcher

Instructors should provide students a written explanation at the beginning of the course concerning the study (See template I in the Appendices of these *Policies & Procedures*), which prominently discloses that students will have an opportunity to agree or not to agree to the inclusion of their data in the instructor's study. The students will be asked to sign the consent form before the end of the course and return it to a third party who will not release the consents until after the end of the course and after grades have been posted. By fashioning the student's participation in this manner, the student is not placed in the position of having to either choose to participate or find an alternative course. Moreover, at the secondary and post-secondary levels of education, election of alternative classes is not likely to be possible.

In situations where the collection of data by a third party is not feasible, the Georgia Tech IRB requires that the students' written consent be obtained by a third party but not released until grades are entered. (See template II in the Appendices of these *Policies & Procedures*).

(Some studies will qualify for a waiver of documentation of consent. For example, a faculty member may ask students to anonymously post comments on an online survey tool regarding instruction methodology. While students will be provided a consent document, the faculty member will not collect signatures or know who participates. In such cases, the IRB recognizes that it is not necessary for a third party to administer consent).

3. Studies Posing Greater Than Minimal Risk to Student Participants

Participation by students in any teaching activity which involves the potential of more than minimal risk (i.e., greater than the risk found in everyday activities) to the student or is unusual or not necessary to the course of study or training in which it occurs, must be accompanied by the student's voluntary, informed consent and must first be reviewed and approved by the full Georgia Tech IRB during a convened meeting prior to commencement of the activity.

4. Additional Points to Consider

a. Group Activities.
Group activities that are required as part of the course instruction pose a particularly difficult situation because the practicality of a student opting out is very limited. If the data is a group project or perhaps a videotape of the group interaction, each student's consent is necessary for the use of that data in the instructor's research. If one student does not consent, the data may be used only if the non-consenting student's data can be effectively excluded. In many cases this will not be possible. Thus, none of the data can be used.

b. Use of Student Grades and Other Assessments
In research where the instructor wants access to identifiable student academic records, signed consent forms are required even if the research activities conducted in the classroom are conducted by a third party and otherwise fall under an exempt category of research. For example, administration of a pre- and post-test by a third party will normally qualify as exempt research under either category 1 or 2, requiring the provision of an information sheet, but not signed consent. If, however, part of the research also includes access to the individual, identifiable student's other grades etc., signed consent from each student is necessary. See section B, below.

c. Minors
Research involving minors (under 18 years of age) as subjects (even 17 year old college students) in most instances requires a signed parental consent. Some types of research may qualify for a *waiver of parental permission*. The Principal Investigator may request a waiver of parental permission; the IRB will determine whether a waiver is appropriate.

d. Graduate Teaching Assistants

Research conducted by graduate students in a class or laboratory in which the student teaches, assists in the class/laboratory, or does any grading is subject to the same restraints described above.

e. Templates to be Utilized in Preparing Consent Documents for Collection of Data by Instructor/Researcher

Two consent templates have been prepared for use by faculty who wish to seek IRB approval to enroll their students in studies. They are located at Appendix 1:

- Template 1: Given to students at beginning of course
- Template 2: To be signed before the end of the course. A third party will hold the consents until after grades are posted, and faculty will not know which students enroll until that time.

f. Circumstances When Class Credit May Be Given to Student Participants

The Georgia Tech IRB has approved the giving of course credit or extra credit to students who participate in research as part of a course requirement only when alternative and equitable means of obtaining credit is made available to students who do not wish to volunteer as research subjects. The Georgia Tech IRB carefully reviews these alternatives to make sure that students are not being coerced into becoming subjects.

Participation in studies may be offered for credit in a class, but students should be given other options for fulfilling the research component that are comparable in terms of time, effort, and educational benefit. To fulfill the research component, students could participate in research, write a brief research paper, or attend faculty research colloquia. The paper should not be graded, and students who attend the colloquia should only have to show up. If students do choose to participate in studies, they should be given several studies from which to choose.

The informed consent statement should make clear the consequences of withdrawing from a project prior to completion (e.g., will credit be given despite withdrawal?). In accordance with federal requirements, participants must be able to withdraw from a study *without penalty*. As a general matter, the Georgia Tech IRB favors giving credit even if the subject withdraws, unless the student withdraws immediately after enrolling and does not begin participation, or there is evidence of bad faith on the part of the student.

B. Disclosure of Students' Personally Identifiable Information from Education Records by an Educational Agency or Institution

The Family Education Rights & Privacy Act (FERPA) establishes specific consent criteria for disclosure of students' personally identifiable information (PII) from education records. Investigators planning to disclose students' PII should consult the Act, from which the following (italicized) guidance is excerpted, and ensure that the proposed consent process adequately addresses these criteria:

> *(a) The parent or eligible student shall provide a signed and dated written consent before an educational agency or institution discloses personally identifiable information from the student's education records, except as provided in § 99.31.*
> *(b) The written consent must:*
> *(1) Specify the records that may be disclosed;*
> *(2) State the purpose of the disclosure; and*
> *(3) Identify the party or class of parties to whom the disclosure may be made.*
> *(c) When a disclosure is made under paragraph (a) of this section:*
> *(1) If a parent or eligible student so requests, the educational agency or institution shall provide him or her with a copy of the records disclosed; and*
> *(2) If the parent of a student who is not an eligible student so requests, the agency or institution shall provide the student with a copy of the records disclosed.*
> *(d) "Signed and dated written consent" under this part may include a record and signature in electronic form that—*
> *(1) Identifies and authenticates a particular person as the source of the electronic consent; and*
> *(2) Indicates such person's approval of the information contained in the electronic consent.*
>
> (Authority: 20 U.S.C. 1232g (b)(1) and (b)(2)(A))
> [53 FR 11943, Apr. 11, 1988, as amended at 58 FR 3189, Jan. 7, 1993; 69 FR 21671, Apr. 21, 2004]

C. Process to Request the Use of Student Data for Research Purposes

The following procedures are to be followed every time FERPA-protected student data are being used for research purposes. These procedures are intended to ensure that requests for FERPA-protected student data are reviewed and approved appropriately and that the source of the data is clear. The roles of the proposer (Principal Investigator), the Institutional Review

Board, the Office of the Registrar, Institutional Research and Enterprise Data Management are outlined below.

1. The proposer contacts the Institutional Review Board for approval to conduct the research.
    a. The Review Board asks the proposer to contact the Registrar to receive permission to receive the student data or to use the student data they already have. All those listed in item 3 below should be copied on the message to the Registrar.
    b. The Registrar reviews and approves the request (or denies the request with explanation) copies the individuals listed below in item 3 in the email response.
    c. If data is needed from IRP, the proposer requests it once the project has approval by the IRB. Communication is always to those listed in item 3 below.

2. The proposer must include the following information in the request:
    a. How is the data going to be collected? Is the proposer requesting that IRP provide the data and, if so, what is the general timeframe within which it is needed?
    b. The reason (briefly) for requesting the data, which would include how the data is going to be used.
    c. State whether the data requested is to be de-identified and explain if student names and GTIDs are to be included.
    d. List the data elements to be included and be prepared to explain why each one is needed for the research.
    e. State how the data will be handled and by whom.
    f. State how the data will be stored while in use.
    g. State how the data will be destroyed when the research is over.
    h. Confirm that the data will not be shared with anyone else, internally or externally.
    i. Confirm that if the results are to be published, proper care is taken to de-identify the data. The identification process should be conducted by someone other than by the proposer.

3. The contacts for Registrar and Institutional Research and Planning are:
    a. Reta Pikowsky, reta.pikowsky@registrar.gatech.edu
    b. Mark Gravitt, mark.gravitt@registrar.gatech.edu
    c. Jason Wang, Jason.wang@irp.gaech.edu
    d. GT IRB, irb@gatech.edu

XIII. Research Involving Georgia Tech Employees (or Consultants) as Participants

Reviewed: July 2024

School employees and laboratory personnel may occasionally participate as subjects in a research project. By virtue of their customary and usual work mission, some research teams routinely design, create, build and test new technologies. It is occasionally difficult to determine when such developmental work crosses over into the realm of human subjects research. In such situations, employees may inadvertently, or even deliberately, become subjects of research. Some indicators that work may require Institutional Review Board approval are:

- The data will be published.
- The data will be used to support an application to the Food & Drug Administration (FDA) for an investigational device exemption.
- The activity is about the subject's behavior, not about function of a test device, instrument or survey.
- Data about the person will be recorded.
- A document, such as a press release, about a new technology will be prepared that describes demonstration of a human diagnostic or therapeutic application.

Georgia Tech employees may not be used as research subjects as a condition of their employment. (Likewise, consultants should not be required to participate as research subjects on projects for which they provide consultant services). Employees (and consultants) should undergo the same IRB-approved consent process that other participants experience.

A. Employees as Vulnerable Participants

In cases where employees or laboratory personnel participate as volunteers in projects being conducted by their supervisor, they represent a vulnerable population. Despite their seeming enthusiasm, school employees and laboratory personnel should not be subjected to even subtle coercion. Investigators must ensure that all personnel who participate in even minimal risk research activities do so entirely voluntarily.

B. Compensation of Participating Georgia Tech Employees and Laboratory Personnel

It is the policy of the Georgia Tech IRB that, if compensation is to be provided for any participants, it should also be provided for those who are Institute employees. Such participants shall be paid through Accounts Payable. If a participant's compensation is greater than the de minimis amount of $75 within a single calendar year, the compensation shall be reported on a 1099-misc/1042. This compensation should not be reported on a W-2, because it is not payment for services performed by an employee.

Employees participating in research studies during the work day should note the special requirements below:

1. Exempt (Salaried) Employees

Employees classified as exempt must have their supervisor's approval to participate in research studies during normal work hours.

2. Non-Exempt (Hourly Paid) Employees

Non-exempt employees must make arrangements to be in the study during lunch or outside of normal work hours. All employees may want to check with the Office of Human Resources regarding the tax implications for participation compensation.

C. Prohibition on Charging Salary (or Consultant Fees) and Participation Compensation to Same Sponsored Project

Employees, graduate students, undergraduate students, or consultants whose compensation is funded by the research grant to which the human subject payments will be charged may not be enrolled as research participants under the associated protocol.

D. Prohibition on Charging an Employee Salary to any Project

Participation in research as a subject is outside the scope of employment of Georgia Tech personnel. Employees who participate as research subjects in studies conducted in their own employment unit must receive whatever compensation non-employees would receive. Offering to pay employees the salary they would have been paid as a matter of course or in lieu of their customary duties is not an appropriate scheme for compensating them as research subjects. Consult the Office of Research Integrity Assurance for assistance.

XIV. Compensation and Incentives for Research Participation

Reviewed: July 2024

Compensation may be in the form of funds, course credit, or other incentive.

A. Purpose of Compensation

Compensation is intended to thank the participant for his time and trouble and to reimburse out-of-pocket expenses associated with participating in the study, such as the cost of transportation and parking, meals away from home, and so on. Compensation might also include certain incentives for participation.

Compensation schemes must be fully described in the protocol, be clearly explained in the consent documents, and be approved by the IRB.

B. Avoidance of Coercion and Undue Influence

It is Georgia Tech policy that compensation for participation in studies shall not constitute an undue influence to participate. Unusually generous payments may blind prospective subjects to the risks of a study or impair their ability to exercise proper judgment, and they may prompt subjects to conceal information that, if known, would prevent their enrolling or continuing as participants in research projects. For example, the indigent may be willing to take greater risks with their health in return for greater compensation.

The Georgia Tech IRB standards for judging whether incentives constitute undue influence must vary according to research procedures and subject populations, but the following questions form the general basis for determining whether incentives are appropriate:

- Are all research conditions in keeping with standards for voluntary and informed consent?
- Are the incentives reasonable and proportional based on the time commitment, complexities and inconveniences of the study and the particular subject population?
- Would a reasonable person consider the incentive to be appropriate?

C. Proration and Bonuses

Proration of compensation is reasonable when participants will be asked to come for several sessions or to stay for several hours. (If there are to be ten 30-minute focus group meetings over two months with a total compensation of $100, participants who withdraw should be compensated at the rate of $10 for each meeting they attended). Participants must be free to withdraw from a study at any time without penalty or loss of benefits to which they are otherwise entitled.

Researchers should construct compensation schemes so that a bonus for completion is not implied. The IRB, however, will approve a bonus scheme that is adequately justified and reasonable. For example, a bonus at the last visit would likely be approved for the study described in the previous paragraph *if, without the final visit, all previously collected data are without value*. In such a case, a proposed compensation plan of $10 per visit and $25 for the final visit would be sufficiently justified and could be approved.

D. Compensation for Participating Children

Compensation for the participation of children should only cover out-of-pocket expenses, since the parent gives permission for the child's participation and receives any monetary compensation. It is reasonable to also give young children a small toy to thank them for their participation.

E. Lotteries and Raffles

It is a felony in the State of Georgia to conduct a lottery, raffle, or similar game of chance without a license. The Georgia Code defines lotteries and raffles as "any scheme or procedure whereby one or more prizes are distributed by chance among persons who have paid or promised consideration for a chance to win such prize." This definition encompasses almost any contest in which something is given away, as long as the participant is required to provide something of value ("consideration"), in exchange for the chance to win. Consideration can be in any form and can be as simple as requiring someone to fill out a survey or questionnaire.

Lotteries and raffles may be lawfully conducted without a license if participants are allowed to enter without having to provide anything of value. For example, if you are asking research participants to complete a questionnaire for a chance of winning $50, you must provide the opportunity to enter the raffle and win the $50 *without* having to actually complete the questionnaire. This can be likened to the "no purchase required" disclaimer in most commercial contests and giveaways.

If the use of a lottery, raffle, or other game of chance is proposed as compensation, the consent form and recruitment materials must state in the compensation section that participation in the research is not required in order to have a chance to win.

F. Other Special Incentives

Occasionally an investigator will propose a contest or competition in order to encourage participation in studies. Examples of those proposed schemes include:

- the elementary school classroom with the most participants may be given an ice cream party,
- the department with the most participants may be given a breakfast buffet, or
- the teacher who signs up the most student participants will receive a $50 gift certificate.

These schemes are evaluated according to their coerciveness, the age and developmental level of participants, the risk level of the study, and so on. In general, these kinds of contests are frowned upon by the IRB.

G. Payment of Referral or "Finder's Fee" for Enrolling Participants

The Georgia Tech IRB has determined that it may be appropriate for investigators to provide a small fee paid to individuals who refer willing human subject research participants. Such fees are paid per individual referral, must be nominal, and may only be used for the recruitment for minimal risk studies. While the IRB approves the general concept of referral fees, the specific use and appropriateness of referral fees will still be considered on a protocol by protocol basis.

1. Such Fees Disapproved for Clinical Studies or Studies of Significant Financial Value or Medical Risk

Such fees may create, or appear to create, a potential conflict of interest in clinical trials or studies having significant financial potential or medical risk. In some cases, individuals may be motivated, or may appear to be motivated, by personal financial interest to refer a subject when such referral might not be of any benefit to the subject. Therefore, it is Institute policy to disapprove the payment of finder's fees for clinical studies or studies having other significant financial value or medical risk.

H. Institute Policy for Departmental Accounting of Payments to Subjects

Senate Bill 300, the Transparency in Government Act, was passed during the state of Georgia 2008 legislative session and was signed by Governor Perdue in May 2008. This bill requires state agencies and state institutions to extract all trade vendor payment data (vendor ID, vendor name, amount & number of payments) to the Department of Audits and Accounts (DOAA). The DOAA will then make these data available to be viewed by the public via a searchable website. *DOAA approved procedures allowing state agencies and state institutions to exclude from this extraction any payments related to human research subjects and/or the Health Insurance Portability and Accountability Act (HIPAA).*

A new account has been created for departments to use for accounting of these types of payments to research subjects. This account will help to better identify these payments and ensure that this private information is not made available on any searchable public websites. Effective July 1, 2009, departments must use the following Account to process payments related to human research subjects and/or HIPAA:

Account-751510 Description-Services - Human Subjects

Questions regarding these payments may be directed to *ap.ask@business.gatech.edu*.

(Note that payments of $600 or more to an individual in a single year necessitate the issuance of IRS 1099s).

1. Compensation to Nonresident Aliens

While research subjects should be compensated for their time and trouble, it is important to remember that such compensation does not constitute wages for services performed. There is no employer/employee relationship between a researcher and a research subject.

US tax law imposes a mandatory withholding of 30% for nonresident alien payments; therefore, all payments made to nonresident aliens must be processed by Accounts Payable, regardless of the amount. If nonresident aliens will be enrolled, the consent document must include the statement that "U.S. Tax Law requires that a 1099-misc be issued if U.S. tax residents receive $600 or more per calendar year. If non-U.S. tax residents receive more than $75, mandatory 30% withholding is required. Your address and Tax I.D. may be collected for compensation purposes only. This information will be shared only with the Georgia Tech department that issues compensation, if any, for your participation."

XV. Research Involving the Use, Collection and/or Storage of Human Biologic Specimens

Reviewed: July 2024

A. Use of Existing Human Tissue, Cell Lines, and Other Stored Samples

Research often involves the use of existing human samples or data. Use of these samples obliges research investigators and the Institutional Review Board (IRB) to consider the rights and welfare of the individuals who provided them, especially when samples retain identifiers or codes. Individuals (sources) who provided samples or from whom information was obtained in the past are no less deserving of protection than are prospective research subjects.

Some research involving the use of cell lines or human tissues may be exempt from submission of IRB materials. The following chart will help you determine whether IRB submission is required. Contact the Office of Research Integrity Assurance for additional guidance.

Type of Cell Line/Tissue Sample	Georgia Tech IRB Requirement
Established cell lines publicly available to qualified scientific investigators [e.g., cell lines commercially available from the American Type Culture Collection (ATCC)], including cell lines that have been published and are available by request from the investigator.	None. Not covered under definition of "human subject."
Cell lines originally obtained from a commercial source (e.g., ATCC) and subsequently modified in the investigator's laboratory	None. Not covered under definition of "human subject."
Samples from deceased individuals or cadaverous tissue	None. Not covered under definition of "human subject." UNLESS genetic testing is to be done AND the tissue has identifiers"
Self-sustaining, cell-free derivative preparations including viral isolates, cloned DNA, or RNA	None. Not covered under definition of "human subject."

B. Definitions

1. **Anonymous Samples:** specimens lacking any code or identifier that would allow a link back to the subject who provided it. *(NOTE:*

Advances in genetic research suggest that anonymity can no longer be assured).

2. **Genetic Research:** any research involving the analysis of human DNA and chromosomes as well as biochemical analysis of proteins and metabolites when the intent of the research is to collect and evaluate information about heritable disease and/or characteristics within a family.
3. **Identifiable/Coded Samples:** specimens that can be linked back to the subject who provided them.
4. **Prospective Collection:** specimens do not exist 'on the shelf' when request is made to Georgia Institute of Technology IRB for approval.
5. **Retrospective Collections:** proposed research involves using specimens that already exist, i.e., already collected and are 'on the shelf', stored or frozen at time of protocol submission to Georgia Institute of Technology IRB.
6. **Third Party:** As referenced below, means that the tissue is not obtained from the human subject directly, but via another source, i.e., tissue bank, Department of Pathology etc. The third party may have the tissue coded with respect to subject identity, but the investigator receives the tissue in an anonymous manner, i.e., no way to link the subject's identity to the tissue once it is in the investigator's hands. Generally, it is good practice for third parties to require proof of Georgia Institute of Technology IRB approval prior to releasing biological specimens to the investigator. *(NOTE: This example is not intended to include the following types of materials which are not covered under the definition of human subject).*
    - Established cell lines publicly available to qualified scientific investigators [e.g., cell lines commercially available from the American Type Culture Collection (ATCC)], including cell lines that have been published and are available by request from the investigator;
    - Cell lines originally obtained from a commercial source (e.g., ATCC) and subsequently modified in the investigator's laboratory;
    - Samples from deceased individuals or cadaverous tissue;
    - Self-sustaining, cell-free derivative preparations including viral isolates, cloned DNA, or RNA;
    - And other commercially available, de-identified biospecimens.

C. Consent and Review Guidelines

Information contained within the following charts is based on the assumption that the only procedure involving human subjects is the collection of biological specimens. Involvement of other procedures may place the activity in a different (higher) review category, and may require consent of the subject where none is required in some cases below.

Waivers of consent are not allowed for FDA regulated studies. Under HHS regulations, a waiver of consent may be permissible when all of the following conditions are met:

I. The research involves no more than minimal risk to the subjects;
II. The research could not practicably be carried out without the requested waiver or alteration;
III. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;
IV. The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
V. Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

The investigator is urged to consult the Georgia Institute of Technology Office of Research Integrity Assurance for more details concerning these issues.

1. Retrospective Collection of Specimen Data

Retrospective Collection: Genetic Research		
Anonymous/Identifiable?	Consent Required?	What Type IRB Review?
Anonymous	No	Expedited
Identifiable	Yes (waived if 3rd party)	Full (Expedited if 3rd party)
Retrospective Collection: Non-Genetic Research		
Anonymous/Identifiable?	Consent Required?	What Type IRB Review?
Anonymous	No	None or Exempt**
Identifiable	Maybe (waived if 3rd party)*	Exempt or Expedited**

**Can request waiver; determination will also be based on purpose of the research.*
***Dependent on the specifics of the protocol.*

2. Prospective Collection of Human Biological Specimens

Collection of biological specimens via procedures performed specifically for research, OR collection of extra biological specimens during a clinically indicated procedure.

Prospective Collection: Genetic Research		
Anonymous/Identifiable?	Consent Required?	What Type IRB Review?
Anonymous	Yes	Expedited or Full*
Identifiable	Yes	Full
Prospective Collection: Non-Genetic Research		
Anonymous/Identifiable?	Consent Required?	What Type IRB Review?
Anonymous	Maybe**	Exempt, Expedited or Full**
Identifiable	Maybe**	Exempt, Expedited or Full**

**Can request waiver; determination will also be based on purpose of the research.*

***Review category depends on procedure to be performed; for e.g., most blood drawing protocols qualify for expedited review. Obtaining an additional biopsy requires review by the full committee.*

3. Prospective Collection of Human Biological Specimens from Future Discarded Clinical Samples

Prospective Collection: Genetic Research		
Anonymous/Identifiable?	Consent Required?	What Type IRB Review?
Anonymous	No	Expedited
Identifiable	Yes (waived if 3rd party)	Full
Prospective Collection: Non-Genetic Research		
Anonymous/Identifiable?	Consent Required?	What Type IRB Review?
Anonymous	No	None or Exempt**
Identifiable	Maybe* (waived if 3rd party)	Exempt, Expedited or Full**

**Can request waiver; determination will also be based on purpose of the research*

***Dependent on the specifics of the protocol.*

D. Points to Be Addressed in the Protocol and Consent Form When Proposing Research on Biological Specimens (including Tissue Banking for Future, Unspecified Research)

See also section XVI of this manual, "Repositories, Tissue Banks and Biobanks; Registries and Data Banks; and Databases."

The National Institutes of Health's National Human Genome Research Institute has provided guidance in the area of informed consent as it relates to genetic/genomic studies. The following is excerpted from that guidance. The full text is available at http://www.genome.gov/10002332:

"…Because of the often profound impact of genetic testing, subjects should be adequately counseled about the specifics of that test. Before an individual agrees to participate in a clinical trial, research project or undergo a genetic test, he or she must be informed of the test's purpose, medical implications, alternatives, and possible risks and benefits. Subjects should additionally be made aware of their privacy rights, including where their DNA will be stored and who will have access to their personal information.

An informed consent document, requiring the patient's signature, should articulate all of these details. Even after signing, the patient may still opt out of the test or study…."

1. Consent for Use, Collection and Storage of Specimens

a. Informed consent must be obtained for the collection of biological specimens AND for any research involving such specimens. Any intention to bank specimens (that is, store them in a biobank or other repository) must be disclosed during the consent *process*, even if the future research use is currently unknown. If the banking of biological specimens is proposed, a separate (additional) consent form for the tissue collection must be used. It must be made clear to potential subjects that their refusal to consent for the research use of biological materials will in no way affect their participation in the instant study or the quality of their clinical care.

2. Confidentiality Issues

Plans for maintaining the confidentiality of specimens must be addressed in the consent document and process. Investigators should consider the physical site for holding the biological specimens, whether it is on or off-campus, and whether it is the individual investigator's specimen repository.

Other issues to be considered include what information will be revealed to whom (subject, subject's family, subject's doctor, employer, insurer, entered into medical record); under what circumstances; and what information may subjects potentially learn (and NOT learn), both about themselves and others.

Will the patient's medical record (MR) be reviewed? If so, the procedures section of the consent form must specifically request access to the medical record.

Who will have access to the samples, and for what purposes? Inform subjects if other investigators will be given access to samples, particularly if specimens will be stored in a tissue bank. Explain how the patient's identity will be kept confidential, specifying if tissue and/or MR data released to other investigators will be linked with personal information (e.g., the patient's name or other personal identifiers) if the tissue/data are released to investigators using the tissue bank. If personal identifiers will be attached, specific consent from the subject must be obtained.

If a new study proposes secondary use of biological specimens, i.e., use of samples collected for a previously conducted study, an assessment will be made by Georgia Tech IRB regarding whether or not the consent that was obtained for the first study is applicable to the second. If the purpose of the new study differs significantly from the purposes stated in the original study, and the specimens are identifiable, obtaining new consent will be required. The Georgia Tech IRB therefore recommends obtaining the initial consent for research with a broadly stated purpose.

Depending on the study aims and risks, the investigator may need to obtain a Certificate of Confidentiality from the NIH. (See the NIH website for guidance).

3. Return of Research Results to Subjects

The protocol should describe anticipated research findings and circumstances that might lead to a decision to disclose the findings to a subject, as well as a plan for how to manage such a disclosure. Protocols proposing disclosure of genetic information to subjects must include counseling of the subject *prior to the subject consenting to participate in the research activity*. This must be addressed in the procedures section of the consent form, as well as in the costs section (i.e., who will pay for the counseling?).

The return of research findings (laboratory tests) should occur only when all of the following apply:

1) The findings are validated by a CLIA-certified laboratory;
2) The findings may have significant implications for the subject's health concerns;
3) A course of action to ameliorate or treat these concerns is readily available; and
4) The subject agreed during the consent process to be informed about validated findings.

If genetic research is proposed, subjects should be informed that they have the right to NOT receive genetic information about themselves. A possible exception involves circumstances where early treatment of a genetically linked disease could improve the subject's prognosis. During the consent process, this eventuality should receive serious contemplation and discussion. The discussion should also address whether subjects consent in advance for the disclosure of important genetic information to relatives.

If results of tests are NOT to be provided to the subjects, explain why not. For example, researchers whose results are not validated by a CLIA-certified laboratory shall not provide research findings to subjects, unless the Institutional Review Board makes a specific exception and approves such return of findings.

4. Risks

What are the non-physical risks that may result from the subject learning about his/her health status (e.g. HIV), or genetic status with respect to a certain disease? These risks include, e.g., questions of paternity, discovery of disease states other than those under study, anxiety, confusion, damage to familial relationships, compromise to the subjects' insurability and employment opportunities. In addition, what is the impact of learning the results from a test if no effective therapy exists? Is psychological stress possible for family members?

Provisions for counseling must be made available to the subject in cases where there are potential psychosocial effects of participation. (The Costs Section of the consent form should address who will pay for such counseling).

Subjects should be informed that there may be risks that are unknown at the time that they give consent.

5. Conflict of Interest

At the time of the proposed activity, if the investigator or the company collaborator/sponsor intends to produce a commercially valuable product, this inherent conflict of interest must be disclosed in the consent form. The disclosure must specify whether or not the subject or his/her heirs will receive a portion of the profits. Note that consent forms cannot contain language through which the subject is made to waive, or appear to waive, any of his/her legal rights.

6. Disposition of Specimens When Subjects Withdraw

The research protocol should address disposition of specimens and the data derived therefrom, if subjects withdraw from the study. One point to consider is whether specimens will be removed from analysis and from any biobanking. See section XVI, "Repositories, Tissue Banks, Biobanks; Registries and Data Banks; and Databases."

7. How Long Specimens Will Be Kept

If specimens are identifiable, specific consent must be obtained from subjects to hold the specimens for a longer period of time. If specimens are unidentifiable (or are rendered unidentifiable by a third party releasing the specimen), it is acceptable for the consent form to say that specimens will be kept for an indefinite amount of time. As a matter of practice, the Georgia Tech IRB recommends that the consent document specifically state that specimens will be kept indefinitely (if unidentifiable).

8. Vulnerable Populations

a. Minors
In genetic studies, these subjects must be considered so as to prevent pressure by family members and the potential for harm that may result from disclosure of genetic information. At least one parent (or legal guardian) must sign a permission form for the banking of a minor's biological specimen.

b. Cognitively Impaired Individuals
Studies on the genetic basis of certain conditions that affect cognition, such as Alzheimer's disease, bring into consideration the competency of the subject to give consent. The competency of the subjects with these conditions should be attested to by a doctor with expertise in the area. Depending on the extent of cognitive impairment, the subject may need a legally authorized representative to decide whether to give consent in this situation.

With minors and cognitively impaired subjects, Georgia Tech IRB may require that assent of the subject be obtained. When appropriate to the research, the consent process should give subjects the option of stating their willingness to be re-contacted.

E. Templates for Consent and Information for Subjects Whose Biological Specimens Are Utilized

The Institutional Review Board has developed sample consent documents and informational brochures to be utilized when consenting subjects for studies

involving the collection of their biological specimens. These materials are located in Appendix 6.

i **If any personal identifiers or code are retained with the specimens:**
(a) *Use the Consent for Storing Blood, Tissue or Body Fluid with Identifying Information* in the Appendices to these *Policies & Procedures* as an addendum to the usual consent form. (If part of a multicenter study, a similar consent form addendum or insert may be substituted.)

(b) Provide each subject with a copy of *Information About Storage and Use of Specimens with Identifying Information* from the Appendices to these *Policies & Procedures*.

ii **If no personal identifiers or code linking the specimen to any subject are retained:**
(a) Use *Consent for Storing Tissue, Blood or Body Fluid without Identifying Information* as an addendum to the usual consent form. (If part of a multi-center study, a similar consent form addendum or insert may be substituted.)
(b) Provide each subject with a copy of *Information About Storage and Use of Specimens Without Identifying Information*.

F. Genetic Information Nondiscrimination Act of 2008

See the Appendices to these *Policies & Procedures* for detailed information on the 2008 Genetic Information Nondiscrimination Act, which provides for limited protections of individual's genetic information. The Act generally prohibits health insurers and employers with more than 15 employees from using genetic information to make decisions about health coverage, insurance premiums, or employment. Employers and health insurers are forbidden to ask about (or make decisions based upon) any genetic data, no matter how long ago the data were collected.

The law does not prohibit genetic discrimination by small employers or by issuers of life insurance, disability insurance, and long-term-care insurance. Because of the risk of discrimination in those contexts, researchers are reminded of their obligations to protect subjects' privacy and to maintain the confidentiality of data. If research participants request information about their personal genetic data, they should be aware that after the data come into their hands, life-insurance companies and small employers might have the right to ask them about the information.

XVI. REPOSITORIES, TISSUE BANKS AND BIOBANKS; REGISTRIES AND DATA BANKS; AND DATABASES

Reviewed: July 2024

Researchers may establish collections of biological specimens or tissues ("materials"), and data with the intent to maintain these over a period of time, to receive additional materials and/or data from multiple sources, and to share them for future research purposes while controlling access to and use of materials and data. Taken together, these activities constitute the establishment of a repository, tissue bank, or biobank; a registry or data bank, or simply a database. The Georgia Tech IRB requires that a protocol be submitted for review and approval prior to the establishment of any of these that will involve human subjects research. For the purposes of this discussion, the following definitions are provided.

A. Definitions

The terms *repository, tissue bank, biobank, registry, data bank*, and *database* are often used interchangeably, although each is somewhat different from the others. These terms, defined below, will be referred to as "repositories" for the purposes of this discussion.

1. ***Repository, Tissue Bank, Biobank:*** A collection of biological specimens or tissues established by a researcher who intends to receive additional specimens or tissues from multiple sources, maintain the specimens or tissues for some period of time, control access to and use of the specimens or tissues which may be used repeatedly for multiple purposes which may evolve over time. A repository, tissue bank, or biobank usually includes additional information about the human subjects from whom the specimens or tissues were obtained. Repositories often maintain codes that link the information and specimens to their donors' identities.

2. ***Registry or Data Bank:*** A registry or data bank is a collection of information elements or databases established by researchers intending to receive and store additional information from multiple sources, maintain the information for an extended period of time,

control access to and use of the information, which may be used repeatedly for multiple purposes which may evolve over time. Information and specimens stored in registries are often linked by codes to the identities of the individuals from whom the information or specimens were obtained.

3. ***Database:*** A database is comprised of information elements arranged for ease and speed of search and retrieval. The information elements (data) may include observations from research studies, medical charts or other records, outcomes for a set of patients with a specific diagnosis, names of potential research subjects, and so on.

B. Procedures for Establishing a Repository

By formally establishing an IRB-approved, non-exempt repository, the repository PI assumes the authority and responsibility for acquiring and sharing data or materials, their approved use and re-use and their secure storage and transfer, as well as for ensuring the proper operation and management of the repository.

The establishment of a non-exempt *repository, tissue bank, registry, data bank*, or *database (hereinafter "repository" or "repositories")* for research purposes must be approved by the Institutional Review Board. The purpose of establishing the repository must be clearly specified in the repository protocol, which must describe the materials or data to be collected and specify their sources. IRB approval may be obtained by submission of a protocol that satisfactorily addresses the several requirements, including the three major elements of a repository:

- Collection of materials or information by contributing investigators,
- Materials and data storage and management ("Repository Operating Procedures"), and
- Use by recipient investigators.

1. Collection of Materials or Data by Contributing Investigators

The process of acquisition must be described, as must the conditions under which data or specimens may be accepted. A Repository Submittal Agreement must be used for acquisition of materials and data. *A sample agreement can be found at Appendix 24.*

a. Consent and Authorization

There must be a process for certifying local IRB approval for each site contributing data or materials to the repository. The process

should require that copies of the local IRB approval letter and consent form or authorization be included in the submission of materials or data to the repository. The local IRB must hold a current Assurance from the federal Office of Human Research Protections.

If materials or data will be prospectively collected and stored for undefined future research uses, including possibly being shared and reused, the consent or authorization form must so state. If collection will be retrospective (that is, the materials and data already exist and are now being assembled into a repository), a waiver of consent or authorization should be approved.

2. Storage and Management of Materials and Data (Repository Operating Procedures)

The repository protocol shall specify not only how and what materials and data will be collected, but also how those will be stored, safeguarded, tracked, and released for use by recipient investigators. The protocol thus should address the following points:

- How access to the materials and data will be controlled, with access to identifiable (uncoded) materials and data restricted to the minimum necessary repository staff;
    - Requirements for staff access and how such access will be monitored;
    - State who else at Georgia Tech will have access to materials and data;
    - Verification as to whether a Certificate of Confidentiality is applicable and, if so, in hand;
- Describe methods for securing and tracking signed Repository Sharing Agreements from recipient investigators;
- Arrangements for the security and confidentiality of materials and data during storage in the repository and during transfer to a recipient researcher;
- The method for identifying materials or data for which consent has been withdrawn including a method to ensure no future use;
- The method for verifying that materials or data are not released when such use would be contrary to existing limitations on future uses, and ensure that future uses are not contrary to those limits; and
- Provide specifically for genetic research "opt out" status for donors who do not want their materials or data used in that kind of research activity.

a. Repository Guardian

A Repository Guardian must be identified by name in the repository protocol. He/she must have completed the training in the protections of human subjects as required by the IRB. The Guardian may also be the Principal Investigator on the repository protocol. The Guardian's responsibilities must be set forth in the repository protocol and must include the following:

- Ensure that materials and data are received and released in accordance with the IRB approved repository protocol;
- Require a Data Use Agreement be executed between the outside Repository and Georgia Tech, when appropriate;
- Execute a Repository Sharing Agreement each time materials or data are released for research purposes;
    - *A sample Repository Sharing Agreement can be found at Appendix 25.*
- Ensure the security and confidentiality of materials and data during storage in the repository and during transfer to a recipient researcher;
- Track acquisition of materials and data and their release to a recipient researcher;
- Ensure that the recipient investigator will not be provided with a key to coded information, ensuring that the recipient investigator shall not be able to re-identify donors;
- Ensure that materials or data for which consent has been withdrawn are not released for future use;
- Verify that materials or data are not released when such use would be contrary to existing limitations on future uses, such as genetic research "opt out", and
- Verify that material transfer agreements are executed when necessary.

b. Security and Confidentiality

The repository protocol must describe adequate procedures to prevent unauthorized access to the repository materials or data. These measures must include the following, as appropriate:

- **Coding:** If data will be coded, the protocol must specify how the code will be safeguarded and who will have access to its key. If materials or data will be released under an IRB-approved waiver of consent or authorization, the collector-investigator must be prohibited from providing the code and key to recipient investigator(s), or otherwise identifying donors, without prior IRB approval.

- **Physical security:** Access to materials and data must be limited to the extent necessary to ensure donors' privacy and confidentiality are protected.
- **Electronic security:** These measures must be reviewed and approved by the Georgia Tech Office of Information Technology.
- **Certificate of Confidentiality:** If a Certificate of Confidentiality (COC) will be obtained, a method must be established to ensure that materials and data shielded under its terms are so marked. The IRB may require that a COC be obtained if the recipient repository has no IRB oversight or when genetic information or specimens will be involved.

3. Release of Materials or Data to Recipient Investigators

Recipient investigators must execute a Repository Sharing Agreement prior to the release of any materials or data by the repository Guardian. Should the recipient investigator wish to access *identifiable* data or materials, his local IRB approval will be required. Each separate study utilizing repository materials or data is considered an individual research activity separate from the repository protocol.

C. Revisions to Repository Protocol

Any proposed revisions to a repository protocol require prior Institutional Review Board approval. Revisions may be submitted for review as *amendments* via IRBWISE.

D. Continuing Approval of Repository Protocol by the Institutional Review Board

Repository Principal Investigators will be required to apply for continuing IRB approval annually.

E. Converting Current Studies to Repositories

The IRB acknowledges that some earlier human research studies may have accumulated data or specimens now thought to be valuable for future research purposes not originally contemplated, and the researcher may wish to convert such study a protocol to a repository. The PI should submit a new repository protocol, citing the original study, and satisfactorily address the procedures for establishing a non-exempt repository. If, during the initial study, subject consent was not obtained for future use of data or materials in a research repository, a waiver of informed consent should be requested.

F. Terminating a Repository

When establishing a repository, the PI should plan for its eventual termination. For example, if the PI should retire, who will oversee the repository's continued operation? Or, will its contents be transferred to a repository located at another site? Will the repository be terminated if funding is no longer available? While these plans may change over time, it is wise to contemplate them when the repository is first established.

When a repository will be terminated, the PI should submit a protocol closure request via IRBWISE. The closure request should describe the disposition of the materials and data, which may be by transfer or donation or even by destruction.

G. Non-Research Repositories or Databases

While the establishment or use of non-research repositories or databases does not constitute *Human Subjects Research* and does not require IRB oversight, IRB review and approval are required for the research use of *identifiable private information* or *identifiable human specimens* from non-research databases and repositories including data/tissue banks and registries.

Even if the researcher believes that the proposed work meets criteria for exemption under 45 CFR 46.104(d), the IRB must follow the federally prescribed method for making the exemption determination.

XVII. Research Using the Internet

Reviewed: July 2024

The internet, for the purpose of this discussion, includes email, websites, bulletin boards, chat rooms, and any other online media or data. When using the internet as a research tool, the following issues must be addressed and incorporated into the protocol and, where appropriate, into the consent process. Internet research considerations can be generally categorized into research participant issues, research design issues, and security issues.

A. Public or Private Space?

While the internet is generally considered a public domain, the expectation of privacy on the internet is relative and largely dependent upon the purpose of users. Participants in a casual online chat room may have little expectation of privacy, while members of virtual communities for vulnerable populations, such as HIV patients or substance abusers, correctly or incorrectly assume some privacy within that community. The online community's purpose and level of accessibility are central to any discussion about informed consent in this environment. Therefore, researchers must be sensitive to how internet users define their online activities.

B. Research Participants

Logistical challenges are posed for researchers using the internet. The good news is that internet research can provide hundreds of participants quickly, and the bad news is that internet research can provide hundreds of participants quickly. Contacting each one to obtain documented consent is impracticable, if not impossible. If research is to be conducted within a specific internet community, such as a support group, the internet site community leader can perhaps be contacted for a discussion of the proposed research and informed consent process. At a very minimum, informed consent should be obtained from the core members of the community. Email is an acceptable medium for the informed consent document.

However, the validation of the virtual informed consent process proves difficult because the direct researcher-subject interaction is missing; the actual age, mental competency and comprehension of the potential subject are not known. The issue of authenticating informed consent via the internet remains

unresolved at this time. At a minimum, though, researchers are encouraged to identify their positions from the outset of the research study.

C. Participation of Minors

Internet research presents a challenge for protecting minors. Internet environments offer no reliable way to confirm the ages of online participants. When recruiting children for an internet study, the IRB generally prefers that parental consent and child's assent be obtained, and researchers will be asked to describe how these are validated. Unfortunately, federal guidance is woefully lacking in this area. Therefore, the IRB will exercise cautious deliberation of any online research specifically involving children.

D. Research Design

Researchers must justify that data collection via the internet is warranted by a research design that is scientifically credible and satisfactorily addresses whether the subject pool adequately represents the study population. For example, the selection of respondents for internet studies could be non-representative due to inherent characteristics of internet use, which could be problematic unless such lack of diversity is intentionally designed into a study. Researchers must state how the identity of participants will be confirmed and whether or how the identity of the researcher will be provided to research participants.

Deception poses special challenges and must be adequately justified. Deception occurs, for example, when a researcher "lurks" in a chat room, giving a false identity and purpose for his participation, but really observing and perhaps recording interactions among other chat room members. When his true purpose and identity are revealed, chat room members may react with anger, feel that their privacy and trust have been assaulted, and suffer anxiety.

Federal regulations permit deception only when a waiver of informed consent is approved by the IRB which has affirmed that risks to subjects are no greater than minimal; the rights and welfare of subjects will not be adversely affected by the waiver; deception is essential in order for the investigator to carry out the research; and at the earliest possible time, subjects must be informed of the nature of the deception and given a reasonable opportunity to withdraw from participation and to have their data excluded. It is exceedingly difficult to ensure that all individuals involved are included in the debriefing process. See Section X of these policies, "Informed Consent, C. Exception to the requirement for Documenting Informed Consent" for a discussion of consent waivers and studies involving deception or concealment.

E. Confidentiality and Privacy

Internet research protocols must specify how anonymity, confidentiality, or privacy will be assured for research participants. Researchers should address the risks and benefits of conducting the study via the internet, including whether participants will incur any costs for their participation (e.g., online time).

The protocol should address whether participants in the study are cooperating voluntarily and that any personal information will be obtained with their knowledge and consent. In general, participants should be fully aware of how the data collected in the study will be used. Research protocols should also assure participants that their information or data will not be used for subsequent non-research purposes such as direct marketing or fundraising.

Researchers must consider potential pitfalls and compromises to data that can occur when using computer and information technology, which can breach participant confidentiality. Forethought should be given to necessary technology, hardware, and software needed to minimize or eliminate problems that might occur. For example, if email data are to be collected, researchers should state whether email identification software is necessary to remove email addresses from respondents or whether Institute firewall protection is adequate. Researchers must also determine whether the informed consent document ought to include information about any of these precautions.

XVIII. Off-Campus Study Locations, including Private Residences, Daycare Facilities, Elementary and Secondary Schools

Reviewed: July 2024

Researchers who wish to conduct research in off-campus locations, including private residences, daycare facilities, or elementary and secondary schools, must comply with the guidance provided here. Study locations, including recruitment sites, must be specified in the protocol.

Please provide written permission to conduct research activities at such sites. Written permission may be by email or on the entity's letterhead. A sample site permission letter is available in the Appendices to these *Policies & Procedures*.

A. Private Residences

Due to risk management issues, the Georgia Institute of Technology IRB prohibits the conduct of research involving human subjects in the private residences of any faculty member or other investigator, student, study staff, family member, or friend. Of course, this policy is not intended to restrict research activities conducted via the internet or telephone, and in which human subjects are not physically present in the private residences of Georgia Tech personnel.

In certain situations, research may be conducted in the home of the research participant. This will require review and approval by the IRB and will depend on the type of research being conducted. If the study will take place in a subject's residence, separate written permission is not required for that purpose. The protocol and consent document must, however, specify that the subject's residence is the study location.

B. Recruitment and Research Conducted in Public and Private Primary or Secondary Schools or Daycare Facilities

Investigators seeking to perform research in schools or daycare facilities must provide written permission from an authorized individual with the protocol submission. In the case of public schools, the investigator must contact the

school district and follow its guidance on securing permission to conduct the research. Many school districts have established policies, and the superintendent's office maintains the authority to approve or disapprove requests. Some school districts, private schools, and daycare facilities have elaborate application processes requiring lengthy lead time and including a criminal background check before permission to conduct research will be granted. Approval must also be obtained from the teacher/direct supervisor of the children.

In cases where the school or daycare has no existing policy on research being conducted with its students, investigators are to contact the principal or head master on site and obtain a signed statement on school letterhead granting permission to conduct the research at the school.

XIX. Research in International Settings

Reviewed: July 2024

A. Review Requirements Differ for Research in Foreign Countries

The U.S. regulations recognize that procedures normally followed in foreign countries (in which the research will take place) may differ from those set forth in the U.S. federal policy. Therefore, research may be approved by a U.S.-based IRB if the procedures prescribed by the [foreign] institution afford protections that are *at least equivalent* to those provided in the U.S. federal policy. The foreign country's procedures may then be substituted for the procedures required by the federal regulations.

Note that the FDA has not adopted the provision, described in the preceding paragraph, for research that it regulates. The FDA regulations were revised in 2008 (§21CFR Part 312.120) to require that Investigational New Drug studies in foreign countries be conducted in accordance with good clinical practice (GCP) rather than in accordance with the Helsinki Declaration or the regulations of the country. GCP standards must be met before the FDA will accept the study in support of an IND or a marketing application.

Students may only conduct minimal risk studies in foreign countries unless the Principal Investigator (faculty) is present and supervising research activities.

B. Local Review and Approval May Be Required Before GT IRB Will Approve

Georgia Tech IRB approval alone does not convey the right or authority to conduct research at a site in another country. Approval from the local IRB or ethics board may be required before final approval is issued by the Georgia Tech IRB. If there is no equivalent IRB or ethics board, investigators may rely on local experts or community leaders to provide approval of the proposed study.

C. Consideration of Local Context and Investigator Experience Important Criteria

The IRB will consider local research context when reviewing international studies to assure protections are in place that are appropriate to the setting in which the research will be conducted. Protocols should contain a description of the investigators' knowledge or experience regarding the culture of the foreign country. Do investigators speak the local language(s), or will a translator be needed?

The IRB may require that an expert consultant evaluate issues of local research context if the IRB does not have a board member with the expertise or knowledge required to adequately evaluate the research in light of local context. In such cases, investigators should provide the IRB with names of individuals qualified to conduct this review, including other members of the Georgia Tech faculty.

D. Consent Issues in Foreign Countries

Since customs differ from country to country, investigators need to be sensitive to local cultural and religious norms when recruiting and enrolling human subjects. For example, signing a consent document for a study collecting opinions about government policy may put subjects at risk in some locales.

The consent process must provide information in a language understandable to the subjects. The process may include a written document or be entirely oral. For those consent forms that must be translated for non-exempt studies, the protocol must contain a *certified affidavit of accurate translation* from an appropriate translator who is unaffiliated with the study. The translated consent form and affidavit must be submitted and approved by the IRB before use of the consent form. Alternatively, departments must provide a charge number so that the Office of Research Integrity Assurance may obtain the certified translations. (NOTE: If the project is not funded, contact the Office of Research Integrity Assurance for assistance with funding translations).

It may be appropriate to orally present informed consent information in conjunction with a short form written consent document. This method involves use of an IRB-approved English language consent form, an IRB-approved short consent form written in the non-English language, and a witness fluent in both English and the language of the subject. A sample short form is provided in the Appendices to these *Policies & Procedures*. The consent form(s) must be submitted to the IRB in English and in a certified translation of the participants' native language. *See Appendix 23 regarding translation.*

Consider the special consent requirements for an illiterate or low-literacy study population. If children or other vulnerable populations will be enrolled, special assent requirements will apply.

Please Note: If the study is considered to be Exempt, certified translations may not be required.

E. Other Issues to Consider for Protocols Conducted in Foreign Countries

Researchers proposing international research should allow additional time for the IRB review process. Consider data protection, storage issues, and safe transport of data. Will collected data be recorded on paper or electronically? It is recommended that personal identifiers not be collected unless essential.

1. Special IRB Considerations for Federally Funded International Research

Approval of federally funded research at foreign institutions engaged in research is only permitted if the foreign institution holds an Assurance with the federal Office for Human Research Protections (OHRP) and if local IRB review and approval is obtained.

2. Review of Research at Foreign Institutions Engaged in Research

When the foreign institution is a performance site *engaged* in research, the IRB will review the proposed protocol to ensure that adequate provisions are in place to protect the rights and welfare of the participants. Because Georgia Tech holds a Federalwide Assurance (FWA) with the Office for Human Research Protections (OHRP), the foreign institution must file an Assurance of compliance with OHRP if the study is federally funded. Federal regulations provide for approval of such research if "the procedures prescribed by the foreign institution afford protections that are *at least equivalent to those provided in §45CFR46*." The Georgia Tech IRB must receive and review the foreign institution IRB (or equivalent) protocol and written approval of each study prior to the commencement of the research at the foreign institution or site. Georgia Tech IRB approval to conduct research at the foreign institution is contingent upon the Georgia Tech IRB receiving a copy of the performance site's IRB (or equivalent) letter of approval.

3. Review of Research at Foreign Institutions Not Engaged in Research

When the foreign institution is a performance site *not engaged* in research and if the foreign institution has an established IRB (or equivalent), the investigator must obtain from the site's IRB (or equivalent) approval to conduct the research at the site. Failing that, the investigator must provide documentation that the site's IRB (or equivalent) has determined that approval is not necessary for the investigator to conduct the proposed research at the site.

When the foreign institution does not have an established IRB (or equivalent), a letter of cooperation must be obtained. This letter must state that the appropriate institutional or oversight officials are permitting the research to be conducted at the performance site. Georgia Tech IRB's approval to conduct research at the foreign institution is also contingent upon receiving a copy of the performance site's IRB (or equivalent) letter of cooperation.

Of course, the Georgia Tech IRB acknowledges that there are some foreign sites that are entirely unable to generate such documentation. The IRB will work with the Georgia Tech researcher to resolve these on a case-by-case basis.

F. Monitoring of Approved International Research

The IRB is responsible for the ongoing review of international research conducted under its jurisdiction. Documentation of regular correspondence between the investigator and the foreign institution may be required. In certain cases, the IRB may require verification from sources other than the investigator that there have been no substantial changes in the research since its last review.

G. Compilation of National Policies

The Office for Human Research Protection (OHRP) has compiled a list of foreign countries that have at least some human subjects research guidelines that may be essentially equivalent to U.S. requirements. Investigators are permitted to substitute the foreign procedures for protecting human subjects except for some FDA-regulated studies. The International Compilation of Human Subject Research Protections) is a listing of the laws, regulations, and guidelines that govern human subjects research in many countries around the world. See http://www.hhs.gov/ohrp/international/index.html.

OHRP Disclaimer: Though this Compilation contains information of a legal nature, it has been developed for informational purposes only and does not constitute legal advice or opinions as to the current operative laws, regulations, or guidelines of any jurisdiction. In addition, because new laws, regulations, and guidelines are issued on a continuing basis, this Compilation is not an exhaustive source of all current applicable laws, regulations, and guidelines relating to international human subject research protections. While reasonable efforts have been made to assure the accuracy and completeness of the information provided, researchers and other individuals should check with local authorities and/or research ethics committees before starting research activities.

XX. Tribal Research

Reviewed: July 2024

Certain precautions are needed when human subjects research will include Tribal populations. If your research involves American Indians or Alaska Natives, your study will be reviewed by the GT IRB and, under some circumstances, one or more additional boards. You will also need to provide the GT IRB with a letter of support from the appropriate authority within each tribe that will be invited to participate in your research.

The following elements should be considered when working with tribal populations:

1. It is not guaranteed that all tribal members will have access to phones (especially long distance calling), email, and/or transportation to and from research visits
2. Any resources that are required from the tribe should be clearly outlined in the letter of support or Tribal Resolution, i.e. meeting space, transportation, use of clinic facilities, staff time, etc.
3. Data ownership during and after the research study should be clearly considered in advance in collaboration with the tribe.
4. Many tribes will want a plan for publication review by the tribe prior to publishing, which should be outlined in the letter of support or Tribal Resolution.

The following steps are to be followed when conducting research with Tribal populations:

Step 1: Obtain letters of support

Each tribe is unique and has their own rules and procedures regarding research within their communities. According to the Indian Health Service's (IHS) IRB, Tribal Council(s) must review research that is taking place within a reservation, at a Tribal facility, or that utilizes any of the Tribe's resources. A letter of support or Tribal Resolution must be obtained from the appropriate authority within the tribe. A letter of support or Tribal Resolution should include a description of the research, a description of any resources that will be provided by the tribe for

the research project, any agreed upon data ownership provisions, and any promises made to the tribe by the study team, as appropriate.

The letter of support or Tribal Resolution must be obtained prior to submitting your application to the IRB for review.

Step 2: Submit your study to the GT IRB

In the research protocol, indicate which tribe(s) will be invited to participate in your study and confirm that once approved, you will submit your study to the additional review boards, as appropriate.

Step 3: Submit your study documents to additional review boards

In an effort to minimize dual review, the GT IRB may rely on a Tribal IRB to provide oversight for research conducted by GT researchers. The GT IRB will explore this option with the appropriate Tribal IRB on a case-by-case basis.

Please refer to the Indian Health Service (IHS) website for additional information and contacts.

Note: IHS will not facilitate collaborations between researchers and tribal communities.

Step 4: Complete your GT IRB submission

Once you have received the necessary permits, approvals, and/or determinations from the appropriate review boards, provide the GT IRB with these documents.

XXI. Regulatory Requirements for Research Subject to the Food & Drug Administration (FDA): Medical Devices or Investigational New Drugs

Reviewed: July 2024

The Food and Drug Administration (FDA) frequently issues new guidance and regulation revisions; thus, the Institutional Review Board will take into account current regulatory guidance in its review of any device or drug studies—at initial and continuing review and when studies are amended.

A medical device is defined by the Food and Drug Administration as *An instrument, apparatus, implement, machine, contrivance, implant, in-vitro reagent or similar or related article, including any component, part or accessory which is:*

- *National Formulary or USP,*
- *Used in diagnosis, cure, mitigation, treatment or prevention of disease,*
- *Does not achieve its primary intended purpose through chemical action. [FDA 92-4173]*

A drug is defined by the Food and Drug Administration as:

- *A substance recognized by an official pharmacopoeia or formulary.*
- *A substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease.*
- *A substance (other than food) intended to affect the structure or any function of the body.*
- *A substance intended for use as a component of a medicine but not a device or a component, part or accessory of a device.*
- *Biological products are included within this definition and are generally covered by the same laws and regulations, but differences exist regarding their manufacturing processes (chemical process versus biological process.)*

A. Responsibilities of All Investigators Conducting Research Subject to the FDA Regulations (§21CFR812.100)

Investigators have numerous responsibilities when conducting research subject to the FDA regulations, including:

- Awaiting IRB approval and any necessary FDA approval before requesting written informed consent or permitting subject participation
- Conducting the investigation in accordance with:
    - the signed agreement with the sponsor
    - the investigational plan
    - the regulations set forth in §21CFR812 and all other applicable FDA regulations, and
    - any conditions of approval imposed by an IRB or FDA
- Supervising the use of the investigational device. An investigator shall permit an investigational device to be used only with subjects under the investigator's supervision. An investigator shall not supply an investigational device to any person not authorized under §21CFR812 to receive it.
- Financial disclosure. A clinical investigator shall disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements under Part 54.
- Disposing of the device properly. Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator shall return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.

1. Maintaining Records (§21CFR812.140)

An investigator shall maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:

a. Correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA

b. Records of receipt, use or disposition of a device that relate to:

(1) the type and quantity of the device, dates of receipt, and batch numbers or code marks

(2) names of all persons who received, used, or disposed of each device

(3) the number of units of the device returned to the sponsor, repaired, or otherwise disposed of, and the reason(s) therefore

c. Records of each subject's case history and exposure to the device, including:

(1) documents evidencing informed consent and, for any use of a device by the investigator without informed consent,

any written concurrence of a licensed physician and a brief description of the circumstances

(2) justifying the failure to obtain informed consent

(3) document all relevant observations, including records concerning adverse device effects (whether anticipated or not), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests

(4) a record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy

d. The protocol, with documents showing the dates of and reasons for each deviation from the protocol

e. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

2. Inspections (§21CFR812.145)

Investigators are required to permit FDA to inspect and copy any records pertaining to the investigation including, in certain situations, those which identify subjects.

3. Submitting Reports (§21CFR812.150)

An investigator shall prepare and submit the following complete, accurate, and timely reports:

a. To the sponsor and the IRB:

(1) Any unanticipated adverse device effect occurring during an investigation. (Due no later than 10 working days after the investigator first learns of the effect.)

(2) Progress reports on the investigation. (These reports must be provided at regular intervals, but in no event less often than yearly. If there is a study monitor, a copy of the report should also be sent to the monitor.)

(3) Any deviation from the investigational plan made to protect the life or physical well-being of a subject in an emergency. (Report is due as soon as possible but no later than 5 working days after the emergency occurs. Except in emergency situations, a protocol deviation requires prior sponsor approval; and if the deviation may affect the scientific soundness of the plan or the rights, safety, or welfare of subjects, prior FDA and IRB approval are required.)

(4) Any use of the device without obtaining informed consent. (Due within 5 working days after such use.)
(5) A final report. (Due within 3 months following termination or completion of the investigation or the investigator's part of the investigation. For additional guidance, see the discussion under the section entitled "Annual Progress Reports and Final Reports.")
(6) Any further information requested by FDA or the IRB about any aspect of the investigation.

b. To the Sponsor:
(1) Withdrawal of IRB approval of the investigator's part of an investigation. (Due within 5 working days of such action).

4. Investigational Device Distribution and Tracking

The IDE regulations prohibit an investigator from providing an investigational device to any person not authorized to receive it (§21CFR812.110(c)). The best strategy for reducing the risk that an investigational device could be improperly dispensed (whether purposely or inadvertently) is for the sponsor and the investigators to closely monitor the shipping, use, and final disposal of the device(s).

Upon completion or termination of a clinical investigation (or the investigator's part of an investigation), or at the sponsor's request, an investigator is required to return to the sponsor any remaining supply of the device or otherwise to dispose of the device as the sponsor directs (§21CFR812.110(e)).

Investigators must also maintain complete, current and accurate records of the receipt, use, or disposition of investigational devices (§21CFR812.140(a)(2)). Specific investigator recordkeeping requirements are set forth at §21CFR812.140(a).

5. Prohibition of Promotion and Other Practices (§21CFR812.7)

The IDE regulations prohibit the promotion and commercialization of a device that has not been first cleared or approved for marketing by FDA. This prohibition is applicable to sponsors and investigators (or any person acting on behalf of a sponsor or investigator), and encompasses the following activities:

a. Promotion or test marketing of the investigational device
b. Charging subjects or investigators for the device a price larger than is necessary to recover the costs of manufacture, research, development, and handling

c. Unduly prolonging an investigation beyond the point needed to collect data required to determine whether the device is safe and effective, and
d. Representing that the device is safe or effective for the purposes for which it is being investigated.

6. Annual Progress Reports and Final Reports

The annual progress and final reports to the sponsor and the IRB must also include the following items:

a. IDE number
b. Device name
c. Indications for use
d. Brief summary of study progress in relation to investigational plan
e. Number of investigators and investigational sites
f. Number of subjects enrolled
g. Number of devices received, used, and the final disposition of unused devices
h. Brief summary of results and conclusions
i. Summary of anticipated and unanticipated adverse device effects
j. Description of any deviations from investigational plan
k. Reprints of any articles published by the investigator in relation to the study

B. Additional Responsibilities of a *Sponsor-Investigator*

A sponsor-investigator, as defined in Food and Drug Administration regulations at §21CFR312.3 and 812.3(o), is an individual who both initiates and conducts a clinical investigation, and under whose immediate direction an investigational drug or device is administered, dispensed or used. A sponsor-investigator has the responsibilities usually assigned both to an investigator and to a sponsor. The IRB will evaluate whether the investigator is knowledgeable about the additional regulatory requirements for sponsors and may require additional oversight and monitoring of such studies to assure compliance with additional sponsor regulations.

Investigators must be trained to recognize device defects which occur from the improper performance of their specific jobs. 21 CFR 820.25(b)(2) states that personnel who perform verification and validation activities shall be made aware of defects and errors that may be encountered as part of their job functions. The sponsor-investigator must provide acceptable evidence that such personnel are adequately trained.

C. Checklist for Studies Involving Investigational Devices:

All protocols that propose testing of investigational devices must satisfactorily address the following points:

- Study Title with Number and Revision Level
- Investigator Credentials, including Medical and State/Federal Licenses, As Required
- Investigational Sites
- Clinical Background of Condition Being Studied
- Study Objective
- Risk Determination (NSR/SR)
- Device Description
    - Description
    - Principles of operation
    - Components and Materials
    - Manufacturing Information
    - Device labels
    - Instructions for Use
    - Operations Manual
    - Import/Export Information
- Report of Prior Investigations
    - Animal Studies
    - Prior Human Studies
    - Bench testing description regarding safety
- Study Design
- Study Population
    - Inclusion/Exclusion Criteria
    - Recruitment Plan
- Study Procedures
- Study Visit Schedule
- Case Report Forms
- Data Collection and Reporting
- Ethical Considerations
    - Human Subjects Protection
    - Informed Consent Form
    - Safety Updates, Any New Information
    - Protocol Amendments
    - Retention of Records
    - Use of Information and Publication
- Statistical Justification and Data Analysis Plan
- Risks and Benefits Analysis

- Safety Assessment
- Data Disclosure and Subject Confidentiality
- Study Monitoring Plan

D. Determining the Safety or Effectiveness of a Device

When a study is designed to evaluate the safety or effectiveness of a device, the convened IRB or the Office of Research Integrity Assurance (if the device fits the criteria to be IDE Exempt) will confirm and document *either that*:

1. The device has a valid IDE number. The IDE for each device must be supported by one of the following:
    - The sponsor protocol imprinted with the IDE number;
    - A written communication from the sponsor documenting the IDE number;
    - A written communication from the FDA documenting the IDE number (required if an investigator listed on this protocol holds the IDE).

OR

2. The device fulfills the requirements for an abbreviated IDE [§21CFR812.2(b)(1)]
    - The device is not a banned device;
    - The device is labeled by the sponsor in accordance with the FDA Investigational Device Exemptions at §21CFR812.5;
    - The sponsor will obtain IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;
    - The sponsor will ensure that each investigator participating in the investigation of the device obtains from each subject under the investigator's care, consent as required by FDA Regulations on the Protection of Human Subjects (§21CFR50) and documents it, unless documentation is waived by the IRB;
    - The sponsor will comply with the requirements of the FDA Investigational Device Exemptions at §21CFR812.46 with respect to monitoring investigations;
    - The sponsor will maintain the records required under the FDA Investigational Device Exemptions at §21CFR812.140(b) (4) and (5) and makes the reports required under the FDA Investigational Device Exemptions at §21CFR812.150(b) (1) through (3) and (5) through (10);
    - The sponsor will ensure that participating investigators maintain the records required by the FDA Investigational Device Exemptions at §21CFR4 812.140(a)(3)(i) and make the reports required under §21CFR812.150(a) (1), (2), (5), and (7); and

- The sponsor complies with the prohibitions in the FDA Investigational Device Exemptions at §21CFR812.7 against promotion and other practices.

OR

3. The device fulfills one of the IDE exemption categories [§21CFR812.2(c)]:

A. The device, other than a transitional device, was introduced into commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time;

B. The device, other than a transitional device, was introduced into commercial distribution on or after May 28, 1976, that FDA had determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that was used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence;

C. The device is a diagnostic device and the sponsor will comply with applicable requirements in §21CFR809.10(c) and the testing:

- Is noninvasive;
- Does not require an invasive sampling procedure that presents significant risk;
- Does not by design or intention introduce energy into a participant;
- Was not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure;

D. The device is undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing was not for the purpose of determining safety or effectiveness and does not put participants at risk;

E. The device is intended solely for veterinary use;

F. The device is shipped solely for research on or with laboratory animals and labeled in accordance with the FDA Investigational Device Exemptions at §21CFR812.5(c);

G. The device is a custom device as defined in the FDA Investigational Device Exemptions at §21CFR812.3(b) and is not being used to determine safety or effectiveness for commercial distribution .

E. Combination Product Studies

As defined in the FDA regulations at §21CFR3.2(e), a combination product is a product composed of any combination of a drug and a device; a biological product and a device; a drug and a biological product; or a drug, device, and a biological product. A combination product is defined to include:

1. A product comprising two or more regulated components (i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic) that are physically, chemically, or otherwise combined or mixed and produced as a single entity;

2. Two or more separate products packaged together in a single package or as a unit comprising drug and device products, device and biological products, or biological and drug products;

3. A drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where, upon approval of the proposed product, the labeling of the approved product would need to be changed (e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose); or

4. Any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

When reviewing studies involving combination products, the IRB considers the Primary Mode of Action (PMOA), as defined in §21CFR3, in its review of the need for an IND and/or IDE for this Combination Product. When it is impossible to determine PMOA, *the primary therapeutic benefit* is considered by the IRB, which is ultimately guided by the FDA's determination of any IND/IDE requirements for the Combination Product.

F. FDA Device Classification

The FDA has established classifications for approximately 1,700 different generic types of devices and grouped them into 16 medical specialties referred to as panels. Each of these generic types of devices is assigned to one of three regulatory classes based on the level of control necessary to assure the safety and effectiveness of the device.

1. The Three Device Classes and Related Requirements

a. Class I General Controls
   - With Exemptions
   - Without Exemptions

b. Class II General Controls and Special Controls
   - With Exemptions
   - Without Exemptions

c. Class III General Controls and Premarket Approval

The class to which a device is assigned determines, among other things, the type of premarketing submission/application required for FDA clearance to market. If a device is classified as Class I or II, and if it is not exempt, a 510k will be required for marketing. All devices classified as exempt are subject to the limitations on exemptions. Limitations of device exemptions are covered under §21CFR Parts 862-892. For Class III devices, a premarket approval application (PMA) will be required unless the device is a preamendment device (that is, it was on the market prior to 1976, or is substantially equivalent to such a device) and PMAs have not been called for. In that case, a 510k will be the route to market.

Device classification depends on the *intended use* of the device and also upon *indications for use*. For example, a scalpel's intended use is to cut tissue. A subset of intended use arises when a more specialized indication is added in the device's labeling such as, "for making incisions in the cornea". Indications for use can be found in the device's labeling, but may also be conveyed orally during sale of the product.

In addition, classification is risk based, that is, the risk the device poses to the patient and/or the user is a major factor in the class it is assigned. Class I includes devices with the lowest risk and Class III includes those with the greatest risk.

As indicated above all classes of devices as subject to General Controls. General Controls are the baseline requirements of the Food, Drug and Cosmetic (FD&C) Act that apply to all medical devices, Class I, II, and III.

2. How to Determine Classification

To find the classification of a device, as well as whether any exemptions may exist, the regulation number for the device must be identified. There are two methods for accomplishing this: go directly to the classification database and search for a part of the device name, or, if

you know the device panel (medical specialty) to which your device belongs, go directly to the listing for that panel and identify your device and the corresponding regulation. You may make a choice now, or continue to read the background information below. If you continue to read, you will have another chance to go to these destinations.

If you already know the appropriate panel you can go directly to the CFR and find the classification for your device by reading through the list of classified devices, or if you're not sure, you can use the keyword directory in the PRODUCT CODE CLASSIFICATION DATABASE. In most cases this database will identify the classification regulation in the CFR. You can also check the classification regulations below for information on various products and how they are regulated by CDRH.
Each classification panel in the CFR begins with a list of devices classified in that panel. Each classified device has a 7-digit number associated with it, e.g., §21CFR880.2920 - Clinical Mercury Thermometer. Once you find your device in the panel's beginning list, go to the section indicated: in this example, §21CFR880.2920. It describes the device and says it is Class II. Similarly, in the Classification Database under "thermometer", you'll see several entries for various types of thermometers. The three letter product code, FLK in the database for Clinical Mercury Thermometer, is also the classification number which is used on the Medical Device Listing form.

Once you have identified the correct classification regulation go to What are the Classification Panels below and click on the correct classification regulation or go to the CFR Search page. Some Class I devices are exempt from the premarket notification and/or parts of the good manufacturing practices regulations. Approximately 572 or 74% of the Class I devices are exempt from the premarket notification process. These exemptions are listed in the classification regulations of §21CFR and also has been collected together in the Medical Device Exemptions document.

G. Determination of Significant and Nonsignificant Risk in Medical Device Studies

The regulations at §21CFR812 discuss Investigational Device Exemptions which include two types of device studies, "significant risk" (SR) and "nonsignificant risk" (NSR). The risk determination has important implications for researchers. Nonsignificant risk device studies have fewer regulatory controls than do SR studies and are governed by the abbreviated requirements [§21CFR812.2(b)].

1. Two Types of Device Studies

a. Significant Risk Device

An SR device study is defined as a study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and

(i). is intended as an implant; or

(ii). is used in supporting or sustaining human life;

or

(iii). is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or

(iv) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

b. Nonsignificant Risk Device

An NSR device investigation is one that does not meet the definition for a significant risk study. *NSR device studies, however, should not be confused with the concept of "minimal risk," a term utilized in the Institutional Review Board (IRB) regulations [§21CFRPart 56] to identify certain studies that may be approved through an "expedited review" procedure.* For both SR and NSR device studies, IRB approval is required prior to conducting clinical trials, and continuing review by the IRB is required. In addition, informed consent must be obtained for both types of studies; the Food & Drug Administration's regulations do not allow for a waiver of consent.

2. Implications of Differences in Significant and Nonsignificant Risk Devices

There are major differences in the approval process and in the record keeping and reporting requirements for SR and NSR studies. The SR/NSR decision is also important to the Food and Drug Administration (FDA) because the IRB serves, in a sense, as the Agency's surrogate with respect to review and approval of NSR studies. FDA is usually not apprised of the existence of approved NSR studies because sponsors and IRBs are not required to report NSR device study approvals to FDA. If an investigator or a sponsor proposes the initiation of a claimed NSR investigation to an IRB, and if the IRB agrees that the device study is NSR and approves the study, the investigation may begin at that institution immediately, without submission of an IDE application to FDA.

If an IRB believes that a device study is significant risk, the investigation may not begin until both the IRB and FDA approve the investigation. To help in the determination of the risk status of the device, IRBs should review information such as reports of prior investigations conducted with

the device, the proposed investigational plan, a description of subject selection criteria, and monitoring procedures. The sponsor should provide the IRB with a risk assessment and the rationale used in making its risk determination.

The assessment of whether a device study presents a NSR is initially made by the sponsor. If the sponsor considers that a study is NSR, the sponsor provides the reviewing IRB an explanation of its determination and any other information that may assist the IRB in evaluating the risk of the study. The sponsor should provide the IRB with a description of the device, reports of prior investigations with the device, the proposed investigational plan, a description of patient selection criteria and monitoring procedures, as well as any other information that the IRB deems necessary to make its decision. The sponsor should inform the IRB whether other IRBs have reviewed the proposed study and what determination was made. The sponsor must inform the IRB of the Agency's assessment of the device's risk if such an assessment has been made. The IRB may also consult with FDA for its opinion.

The IRB may agree or disagree with the sponsor's initial NSR assessment. If the IRB agrees with the sponsor's initial NSR assessment and approves the study, the study may begin without submission of an IDE application to FDA. If the IRB disagrees, the sponsor should notify FDA that an SR determination has been made. The study can be conducted as an SR investigation following FDA approval of an IDE application. The risk determination should be based on the proposed use of a device in an investigation, and not on the device alone. In deciding if a study poses an SR, an IRB must consider the nature of the harm that may result from use of the device. Studies where the potential harm to subjects could be life-threatening, severely debilitating, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure should be considered SR. Also, if the subject must undergo a procedure as part of the investigational study, e.g., a surgical procedure, the IRB must consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.

FDA has the ultimate decision in determining whether a device study is SR or NSR. If the Agency does not agree with an IRB's decision that a device study presents an NSR, an IDE application must be submitted to FDA. On the other hand, if a sponsor files an IDE with FDA because it is presumed to be an SR study, but FDA classifies the device study as NSR, the Agency will return the IDE application to the sponsor and the study would be presented to IRBs as an NSR investigation.

An investigation of a device submitted to FDA for risk determination may not begin until thirty days after FDA receives the application at the address in 812.19 for the investigation of a device other than a banned device, unless FDA notifies the sponsor that the investigation may not begin; or until FDA approves, by order, an IDE for the investigation.

a. Nonsignificant Risk IDE Abbreviated Requirements

The following categories of investigations are considered to have approved applications for IDE's, unless FDA has notified a sponsor under 812.20(a) that approval of an application is required:

(1) An investigation of a device other than a significant risk device, if the device is not a banned device and the sponsor:

(i) Labels the device in accordance with 812.5;

(ii) Obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;

(iii) Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under part 50 and documents it, unless documentation is waived by an IRB under 56.109(c).

(iv) Complies with the requirements of 812.46 with respect to monitoring investigations;

(v) Maintains the records required under 812.140(b) (4) and (5) and makes the reports required under 812.150(b) (1) through (3) and (5) through (10);

(vi) Ensures that participating investigators maintain the records required by 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5),and (7); and

(vii) Complies with the prohibitions in 812.7 against promotion and other practices.

b. Significant Risk IDE Requirements

When the IRB determines that a device is “Significant Risk” (per 812.66), the Investigational Device Exemption (IDE) application shall include, in the following order:

(1) The name and address of the sponsor.

(2) A complete report of prior investigations of the device and an accurate summary of those sections of the investigational plan described in 812.25(a) through (e) or, in lieu of the summary, the complete plan.

The sponsor shall submit to FDA a complete investigational plan and a complete report of prior investigations of the device if no IRB has reviewed them, if FDA has found an IRB's review inadequate, or if FDA requests them.

(3) A description of the methods, facilities, and controls used for the manufacture, processing, packing, storage, and, where appropriate, installation of the device, in sufficient detail so that a person generally familiar with good manufacturing practices can make a knowledgeable judgment about the quality control used in the manufacture of the device.

(4) An example of the agreements to be entered into by all investigators to comply with investigator obligations under this part, and a list of the names and addresses of all investigators who have signed the agreement.

(5) A certification that all investigators who will participate in the investigation have signed the agreement, that the list of investigators includes all the investigators participating in the investigation, and that no investigators will be added to the investigation until they have signed the agreement.

(6) A list of the name, address, and chairperson of each IRB that has been or will be asked to review the investigation and a certification of the action concerning the investigation taken by each such IRB.

(7) The name and address of any institution at which a part of the investigation may be conducted that has not been identified in accordance with paragraph (b)(6) of this section.

(8) If the device is to be sold, the amount to be charged and an explanation of why sale does not constitute commercialization of the device.

(9) A claim for categorical exclusion under 25.30 or 25.34 or an environmental assessment under 25.40.

(10) Copies of all labeling for the device.

(11) Copies of all forms and informational materials to be provided to subjects to obtain informed consent.

(12) Any other relevant information FDA requests for review of the application.

H. Control, Handling and Documentation of Devices Used in Investigations

As part of the protocol submission, investigators must provide a description of the planned process for control, handling and documentation of devices investigated or evaluated in the proposed research study. A member of the IRB will evaluate whether the proposed plan is adequate.

I. Case Report Forms

As the principal mechanism for clinical trials data collection, Case Report Forms (CRFs) can directly affect the success or failure of a clinical trial. The information captured in CRFs is used to evaluate each question posed by the study. *The clinical trial sponsor (sponsor-investigator) is responsible for developing an appropriate CRF for the clinical trial in which it will be used.* CRFs must be finalized before data collection begins and should:

- Collect data with all users in mind;
- Collect data required by the regulatory agencies;
- Collect data outlined in the protocol;
- Be concise and clear as to meaning;
- Avoid duplication;
- Allow for minimal free-text responses;
- Provide units to ensure comparable values;
- Provide instructions to reduce misinterpretations
- Provide choices for each question;
- Allow for "*none*" and "*not done*" as responses; and
- Collect data in a manner that supports efficient computerization.

J. Protocols Proposing the Study of Investigational New Drugs

Investigators who contemplate research involving investigational new drugs (INDs) must contact the Office of Research Integrity Assurance prior to preparation of such protocols. This situation is highly unlikely to arise on a study conducted in Georgia Tech facilities, given the typical human studies

conducted by Georgia Tech faculty. Georgia Tech does not have a medical school, but does considerable collaboration with other medical colleges and hospitals.

XXII. Health Insurance Portability and Accountability Act (HIPAA) for Protected Health Information

Reviewed: June 2024

Personal health information that is not obtained from a covered entity, that is self-disclosed by research participants, and that is kept only in the researcher's records is not subject to HIPAA but is regulated by other human subjects protection regulations.

The Department of Health and Human Services' *National Standards to Protect the Privacy of Personal Health Information* are promulgated in the Health Insurance Portability and Accountability Act (HIPAA) of 1998, commonly referred to as the "Privacy Act." This Act specifies requirements for protection of individually identifiable health information (IIHI) or "protected health information" (PHI). PHI is individually identifiable health information (IIHI) such as name, address, social security number, email address, telephone number, etc., that is created, received or maintained by a Covered Entity (CE). A CE is a Health Care Provider that performs one of the standard electronic transactions identified in the HIPAA Privacy Rule; a Health Plan; or a Health Care Clearinghouse. Virtually all doctors, hospitals, and other health care facilities are Covered Entities.

A. Definitions

For the purposes of this discussion, it is important to understand certain definitions within the context of HIPAA:

1. Covered Entity

Covered entities are health care providers *(if they transmit any information in an electronic form in connection with a transaction for which HHS has adopted a standard)*, health plans, health care clearinghouses, and their business associates.

2. Hybrid Entity

Georgia Tech is a hybrid entity, with only portions of the Institute subject to HIPAA. As a hybrid entity, any individually identifiable health information maintained by other components of the

university (i.e., outside of the health care component), such as a law enforcement unit, or a research department, would not be subject to the HIPAA Privacy Rule, notwithstanding that these components of the institution might maintain records that are not "education records" or treatment records under FERPA.

3. Authorization (Consent)

(Patient) authorization is the HIPAA equivalent of consent to use and disclose (patient) data.

4. Protected Health Information (PHI)

Protected health information includes all *individually identifiable* health information transmitted or maintained by an organization covered by the HIPAA regulations (a "covered entity"), regardless of form. Specifically, if it is Individually Identifiable Health Information (IIHI) that is:

- created or received by a health care provider, health plan, employer, or health care clearinghouse; **AND**
- personal health information that relates to:
    - the past, present, or future physical or mental condition,
    - the past, present, or future provision of care to an individual, or
    - the past, present or future payment for provision of health care to an individual, and
    - identifies the individual (or there is a reasonable basis to believe that the information can be used to identify the individual).

Health-related information is PHI if:

- The researcher obtains the information from a healthcare provider, health plan, health clearinghouse, business associate, or employer (other than records solely relating to employment status;

OR

- The records were created by a healthcare provider, health plan, health clearinghouse, or employer, AND the researcher obtains the records from an intermediate source which is not a school or employer record related solely to employment status;

OR

- The researcher obtains the records directly from the study subject in the course of providing treatment to him.

Health-related information is not considered PHI if the researcher obtains it from:

- Student records maintained by a school;

OR

- Employee records maintained by the employer for employment status;

OR

- The research subject directly, if the research does not involve treatment.

B. What Research Is Subject to the HIPAA Regulations?

Any research conducted under the auspices of Georgia Tech that creates, uses, or discloses protected health information obtained from a covered entity is subject to the Health Insurance Portability and Accountability Act (HIPAA). .

C. Types of Health Information

There are three categories of health information. The requirements for use are different for each.

1. Individually Identifiable Health Information (IIHI)

IIHI includes any subset of health information, including demographic information collected from an individual, that:

- Identifies the individual (or there is a reasonable basis to believe that the information can be used to identify the individual.)
- The general rule is that an authorization signed by the research subject is required for the disclosure of individually identifiable health information. An IRB may waive this requirement.

2. De-Identified Data Sets

Health information is considered de-identified when it does not identify an individual and the covered entity has no reasonable basis to believe that the information can be used to identify an individual. Information is considered de-identified if 18 identifiers are removed from the health information and if the remaining health information could not be used alone, or in combination, to identify a subject of the information. An IRB may waive authorization for the use of de-identified data.

The 18 identifiers that may not be included in de-identified data sets are:

1. Names;
2. All geographical subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the

initial three digits of a zip code, if according to the current publicly available data from the Bureau of the Census:

- The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and
- The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.

3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older;
4. Phone numbers;
5. Fax numbers;
6. Electronic mail addresses;
7. Social Security numbers;
8. Medical record numbers;
9. Health plan beneficiary numbers;
10. Account numbers;
11. Certificate/license numbers;
12. Vehicle identifiers and serial numbers, including license plate numbers;
13. Device identifiers and serial numbers;
14. Web Universal Resource Locators (URLs);
15. Internet Protocol (IP) address numbers;
16. Biometric identifiers, including finger and voice prints;
17. Full face photographic images and any comparable images; and
18. Any other unique identifying number, characteristic, or code (This does not refer to the unique code assigned by the investigator to code the data).

3. Limited Data Sets

A *limited data set* is information disclosed by a covered entity to a researcher who has no relationship with the individual whose information is being disclosed. The covered entity is permitted to disclose PHI, with direct identifiers removed, *subject to obtaining a data use agreement from the researcher receiving the limited data set*. The PHI in a limited data set may not be used to contact subjects. The IRB may waive authorization for use of limited data sets in research.

Direct identifiers that must be removed from the information for a limited data set are:

1. Name,
2. Address information (other than city, State, and zip code),
3. Telephone and fax numbers,
4. E-mail address,
5. Social Security number,
6. Certificate/license number,
7. Vehicle identifiers and serial numbers,
8. URLs and IP addresses,
9. Full face photos and other comparable images,
10. Medical record numbers, health plan beneficiary numbers, and other account numbers,
11. device identifiers and serial numbers,

12. biometric identifiers including finger and voice prints.

Identifiers that are allowed in the limited data set are:

1. Admission, discharge and service dates,
2. Birth date,
3. Date of death,
4. Age (including age 90 or over),
5. Geographical subdivisions such as state, county, city, precinct and five digit zip code.

D. Authorization (Consent) Requirements

HIPAA regulations use the term "authorization" to describe the process through which a patient consents for researchers to access protected health information. Blanket authorizations for research to be conducted in the future are not permitted. Each new use requires a specific authorization. The authorization for disclosure and use of protected health information may be combined with the consent form that a research subject signs before agreeing to be in a study. It may also be a separate form. In either case, the information must include:

1. Elements of Required Authorization

- A description of the information to be used for research purposes;
- Who may use or disclose the information
- Who may receive the information
- Purpose of the use or disclosure
- Expiration date of authorization
- How long the data will be retained with identifiers
- Individual's signature and date
- Right to revoke authorization
- Right to refuse to sign authorization (if this happens, the individual may be excluded from the research and any treatment associated with the research)
- If relevant, that the research subject's access rights are to be suspended *while the clinical trial is in progress*, and that the right to access PHI will be reinstated at the conclusion of the clinical trial.
- That information disclosed to another entity in accord with an authorization may no longer be protected by the rule.

2. Waiver of Authorization for Research

The Institutional Review Board uses the following criteria in approving requests for a waiver of authorization for research:

- The use or disclosure of protected health information must involve no more than minimal risk to the privacy, safety, and welfare of the individual;
- The research could not practicably be conducted without the waiver or alteration; and
- The research could not practicably be conducted without access to the protected health information.

The Institutional Review Board must also consider if the researcher has provided:

- an adequate plan to protect the identifiers from improper use or disclosure;
- an adequate plan to destroy the identifiers at the earliest opportunity, unless retention of identifiers is required by law or is justified by research or health issues; and
- adequate written assurance that the PHI will not be used or disclosed to a third party except as required by law or permitted by an authorization signed by the research subject.

E. Information Needed for Review by the IRB

Detailed information is needed about the types of information investigators will use in their research, how it will be used, who will have access to it, and when it will be destroyed. Specifically, researchers should address:

- What risks are posed by the use of the data and how have they been minimized?
- What is the justification for access to the data and why are they necessary to conduct the research?
- What plan does the researcher have to protect identifiers from improper use or disclosure?
- What is the researcher's plan to destroy the identifiers? If it is not possible to destroy the identifiers, what is the health, legal, or scientific justification?
- Has the researcher provided adequate written assurance that the PHI will not be used or disclosed to a third party except as required by law or permitted by an authorization signed by the research subject?

Researchers requesting waivers of authorization will need to explain that the use or disclosure poses no more than minimal risk to the subject; that the research could not practicably be conducted without the waiver; and that the research could not practicably be conducted without access to the protected health information. The researcher must explain:

- how the use of PHI involves no more than minimal risk to individuals

- why such a waiver will not adversely affect privacy rights or welfare of individuals in the study
- why the study could not practicably be conducted without a waiver
- why it is necessary to access and use protected health information to conduct this research
- how the risks to privacy posed by use of PHI in this research are reasonable in relation to the anticipated benefits
- the plan to protect identifiers from re-disclosure
- the plan to destroy identifiers. Provide a date by which this will take place. If identifiers must be retained, provide the reason (scientific, health, or other) why this is necessary.
- and confirm that the PHI will not be reused or disclosed to anyone else.

F. Human Subjects' Rights

1. Right to an Accounting

When a research subject signs an authorization to disclose PHI, the covered entity is not required to account for the authorized disclosure. An accounting is not required when the disclosed PHI was contained in a limited data set or is released to the researcher as de-identified data. However, an accounting is required for research disclosures of identifiable information obtained under a waiver or exception of authorization. Research subjects may request an accounting of disclosures going back for up to six years.

2. Right to Revoke Authorization

A research subject has the right to revoke their authorization unless the researcher has already acted in reliance on the original authorization. Under the authorization revocation provision, covered entities may continue to use or disclose PHI collected prior to the revocation as necessary to maintain the integrity of the research study. Examples of permitted disclosures include submissions of marketing applications to the FDA, reporting of adverse events, accounting of the subject's withdrawal from the study and investigation of scientific misconduct.

G. Subject Recruitment

1. Recruitment is Subject to the General Authorization Requirements

The Privacy Rule classifies recruitment as "research" rather than as health care operations or marketing. Because development or use of

research databases falls within the definition of "research," a covered entity may disclose PHI in a database to sponsors for subject recruitment only after an authorization from the research subject or a waiver from the Institutional Review Board has been obtained.

2. Requirements to Disclose PHI Contained in a Limited Data Set or as De-Identified Data

It is easier to create databases of potential subjects' limited data sets to verify feasibility to conduct a clinical trial or to perform epidemiological research.

3. Limitations on Use of PHI in a Limited Data Set for Subject Recruitment

The PHI may not be used to contact subjects, and, because telephone numbers, internet provider addresses, and email addresses are not part of a limited data set, this information may not be collected by researchers from prospective subjects.

4. Recruiting Subjects Identified using their PHI

When researchers want to approach potential subjects to participate in a study who they have identified using PHI under a waiver of authorization, they must use an approach method that has been approved in advance by the IRB. Examples include using an intermediary such as the patient's primary care provider or a member of the medical staff actually caring for that patient, or sending the potential subject a letter signed by the patient's provider.

H. Requirements for Security of Protected Health Information under the Health Insurance Portability and Accountability Act (HIPAA)

All investigators performing human subject research that involves access to Protected Health Information (PHI) are required to comply with both the Privacy Rule and Security Rule of the Health Insurance Portability and Accountability Act (HIPAA).

The Office of Research Integrity Assurance and the Office of Information Technology (OIT) have partnered to ensure that researchers utilizing PHI are able to adequately safeguard those data. All researchers needing access to PHI shall complete the CITI HIPAA Privacy Rule training beforehand. Therefore, investigators who create, use or otherwise obtain individually identifiable health information are asked to:

1. Complete the HIPAA Privacy Rule training module at on CITI (information required training), and

2. Undergo a data security assessment conducted by the Office of Information Technology. (The Office of Research Integrity Assurance will inform OIT when such protocols are submitted; OIT will contact investigators directly to schedule assessment).

Only those computer terminals conforming to the Institute's HIPAA Rule Security Standards may be used for the creation, receipt, or maintenance of PHI. See also Appendix 4 of these *Policies & Procedures*, "*Data Storage Guidelines*."

With these provisions in mind, the Georgia Tech IRB requires that investigators who create, use or otherwise obtain PHI provide more detailed information about data storage, security, planned re-disclosure, and destruction; and provide more information to research subjects in the consent and authorization process about their PHI will be used.

It is a violation of this policy for any person performing work with PHI for Georgia Tech as an employee or independent contractor to fail to comply with any Privacy and/or Security Rule obligation for which they are responsible, regardless of whether such failure is intentional or not.

1. HITECH Act of 2009

On April 17, 2009, the Department of Health and Human Services (HHS) issued guidance specifying the technologies and methodologies that render protected health information unusable, unreadable, or indecipherable to unauthorized individuals, as required by the Health Information Technology for Economic and Clinical Health (HITECH) Act passed as part of the American Recovery and Reinvestment Act of 2009 (ARRA). This guidance was developed through a joint effort by the Office of Civil Rights, the Office of the National Coordinator for Health Information Technology, and the Centers for Medicare and Medicaid Services.

There are two breach notification regulations, one issued by HHS for covered entities and their business associates under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) (Sec. 13402 of HITECH), and the other issued by the Federal Trade Commission (FTC) for vendors of personal health records and other non-HIPAA covered entities (Sec. 13407 of HITECH).

2. Strengthened Enforcement Measures

Perhaps the most significant feature of the HITECH Act is the strengthening of HIPAA enforcement measures. Whereas the Office of Civil Rights (OCR) and the Department of Justice were the only HIPAA

enforcement authorities previously, the Act authorizes state Attorneys General to enforce HIPAA violations in federal court. Should the Department of Justice not pursue criminal penalties for a violation that constitutes criminal behavior, the Office of Civil Rights is now authorized to pursue civil penalties for the same violation.

The Act includes new civil and criminal penalties for employees, with monetary fines being returned to OCR for future enforcement purposes and, eventually, to compensate victims. Civil monetary penalties for willful neglect violations were previously maxed at $25,000; the Act tiers civil monetary penalties with a maximum of $1.5 million.

XXIII. Projects Conducted by Multiple Faculty, or at Multiple Sites, or by Subrecipients

Reviewed: July 2024

THIS POLICY DOES NOT APPLY WHEN A DOD AGENCY IS THE SPONSOR.*

The Department of Defense (DOD) agencies, including DOD, Air Force, Army, Navy, Marines, Coast Guard, and others, will not award funds for human research work unless the center grant/contract Principal Investigator is named as a member of the research team in the human research protocol. In most cases, the center grant/contract Principal Investigator may be named as co-Principal Investigator in the research protocol. The investigator must also complete the required CITI modules that other members of the protocol research team must complete.

**NOTE: Intelligence Advanced Research Projects Activity (IARPA) and Veterans Administration are not DOD components.*

The Institutional Review Board recognizes that large Program or Center grants may fund multiple projects conducted by multiple Georgia Tech faculty or entirely at other research sites and that have no direct involvement of the grant Principal Investigator. The following policy has been established to facilitate IRB approvals in such cases.

A. Program or Center Grants that Fund Projects Conducted by Multiple Faculty Members at Georgia Tech

If the Program/Center grant Principal Investigator has absolutely no involvement in the human research supported by the grant and conducted by other Georgia Tech faculty members, the Principal Investigator does not need to submit a protocol for IRB review. Instead, the Principal Investigator should inform their subrecipients that they are responsible for obtaining IRB approval, if needed, and follow-up to ensure that such required approvals are obtained.

1. IRB Responsibilities of Georgia Tech Faculty Whose Human Subjects Research Is Funded By an Program or Center Grant

Faculty members whose human research activities are funded by the program or center grant are responsible for securing Georgia Tech's IRB approval for their human subjects research prior to its initiation. Their protocols shall indicate funding by the program or center grant, and they shall provide their Georgia Tech IRB protocol approval letters to the program or center grant Principal Investigator.

2. Grants and Contracts Accounting for Sub-Projects

These "sub-projects" are further administered for budgetary purposes by the Office of Grants and Contracts Accounting, which establishes separate funds for each one. See those policies on the Grant and Contracts Accounting website.

B. Program or Center Grants That Fund Projects Conducted at Non-Georgia Tech Sites and the Georgia Tech Principal Investigator Has No Direct Interaction with Human Subjects

This guidance is for situations in which the subrecipient(s)'s Institutional Review Board is registered with the Office for Human Research Protections and holds a current Federalwide Assurance.

Occasionally, a Program or Center grant to a Georgia Tech Principal Investigator will fund multi-site research involving human subjects with which the Georgia Tech PI will have no direct interaction, even if Principal Investigator receives de-identified human subjects data from the other sites. In such cases, the GT PI does not need to submit a protocol for IRB review. Instead, the Principal Investigator should inform subrecipients that they are responsible for obtaining IRB approval at their institutions where the human research activities will take place and provide a copy of their IRB letter of approval to the GT PI.

The GT PI must submit the subrecipient(s)'s letter of IRB approval to the Georgia Tech Office of Research Integrity Assurance, which will work with the recipient IRB to execute an Interinstitutional Authorization Agreement (IAA), whereby the Georgia Tech IRB defers to the recipient IRB.

Should GT PI learn that adverse events occur at the other site, the Georgia Tech PI shall bring those to the attention of the Georgia Tech IRB.

C. Program or Center Grants That Fund Projects Conducted at Non-Georgia Tech Sites and the Georgia Tech Principal Investigator HAS Direct Interaction with Human Subjects

This guidance is for situations in which the subrecipient's Institutional Review Board is registered with the Office for Human Research Protections and holds a current Federalwide Assurance.

In the event that the human research is to be conducted in part by Georgia Tech investigator(s) and in part by a subrecipient, the Georgia Tech investigator must submit to the Office of Research Integrity Assurance for IRB review a protocol clearly describing the work to be conducted by the subrecipient and that to be conducted by Georgia Tech investigator(s). The subrecipient's letter of IRB approval from his home institution must be included. If it determines that an Interinstitutional Authorization Agreement (IAA) is required, the Georgia Tech Office of Research Integrity Assurance will coordinate with the subrecipient(s)'s IRB to secure the IAA.

In these cases, the Georgia Tech investigator will serve as Principal Investigator. The PI shall also inform the IRB if they have a conflict of interest, in which case assistance will be provided to ensure the conflict is appropriately managed. No subaward will be issued by Georgia Tech's Office of Sponsored Programs until the subrecipient's IRB and the Georgia Tech IRB have approved the work.

D. Other Projects Subbed to Non-Georgia Tech Sites Wanting to Rely on the Georgia Tech Institutional Review Board

In some cases, the subrecipient institution, regardless of whether it has its own OHRP-approved Assurance, may wish to rely on a review by the Georgia Tech IRB. Interinstitutional Authorization Agreements (IAAs) are established on a case-by-case basis and only with the approval of the Institutional Official. When appropriate, the Office of Research Integrity Assurance will execute an IAA describing the subrecipient's reliance upon the Georgia Tech IRB.

The Georgia Tech IRB will follow written procedures for reporting its findings and actions to appropriate officials at the relying institution. Relevant minutes of IRB meetings shall be made available to the relying institution upon request.

The relying institution's researchers must present documentation of having completed the required training in human research participant protections or, within thirty days of the execution of the IAA, satisfactorily complete the training provided by the Georgia Tech IRB. The relying institution will promptly and immediately forward to the Georgia Tech IRB any information regarding safety, adverse events, or other relevant data. The relying institution will also provide to Georgia Tech IRB any relevant correspondence between itself and the sponsor, the Office for Human Research Protections or the Food & Drug Administration. The relying institution remains responsible for ensuring compliance with the Georgia Tech IRB's determinations and policies and with the terms of its OHRP approved Federalwide Assurance.

XXIV. Reciprocal Agreements with Emory University, St. Joseph's Hospital, Children's Hospital of Atlanta, and the University of Georgia for Deferring IRB Review in Certain Cases; Consent Harmonization with Shepherd Center

Reviewed: July 2024

In recognition of the many collaborative partnerships between Georgia Tech researchers and those from neighboring institutions, a number of reciprocal agreements have been established.

A. Emory University and Georgia Institute of Technology Reciprocal Agreement

Emory University and Georgia Tech have executed an Interinstitutional Authorization Agreement (IAA) setting forth the terms and conditions under which Emory and GT may rely on the other for IRB review.

1. Student Research

If a protocol is initiated by a Georgia Tech student who is working on the protocol with a PI whose home institution is Emory or a Georgia Tech student wishes to join the research team on a protocol initiated by a PI whose home institution is Emory, and the protocol activities (excluding data analysis) are to be completed at an Emory site, then the Georgia Tech IRB shall rely upon the Emory IRB for review and oversight of the protocol.

If a protocol is initiated by an Emory student who is working on the protocol with a PI whose home institution is Georgia Tech or an Emory student wishes to join the research team on a protocol initiated by a PI whose home institution is Georgia Tech, and the protocol activities (excluding data analysis) are to be completed at a Georgia Tech site, then the Emory IRB shall rely upon the Georgia Tech IRB for review and oversight of the protocol.

If a protocol is initiated by either a Georgia Tech or Emory student and the protocol activities (excluding data analysis) take place both at Emory and Georgia Tech sites, then both the Emory and the Georgia Tech IRBs shall be responsible for review and oversight of the protocol.

See also Policy Statement VI.C., *"Eligibility Exceptions for Graduate and Undergraduate Students as Principal Investigators."*

2. Faculty/Staff Research

If a PI or co-investigator on a protocol has Georgia Tech as a home institution, but the protocol activities (excluding data analysis) take place at an Emory site, then the Georgia Tech IRB shall rely upon the Emory IRB for review and oversight of the protocol.

If a PI or co-investigator on a protocol has Emory as a home institution, but the protocol activities (excluding data analysis) take place entirely at a Georgia Tech site, then the Emory IRB shall rely upon the Georgia Tech IRB for review and oversight of the protocol.

If the PI on a Protocol has either Emory or Georgia Tech as a home institution, and the protocol activities (excluding data analysis) take place at both Emory and Georgia Tech Sites, then both the Emory IRB and the Georgia Tech IRB shall be responsible for review and oversight of the protocol.

3. Protected Health Information

In accordance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and notwithstanding anything to the contrary above, if the protocol activities (including data analysis) involve the use and/or disclosure of Protected Health Information from Emory University's covered entity, then the Emory IRB, acting as privacy board, shall review the protocol solely for HIPAA Privacy Rule purposes.

4. Individual Interinstitutional Authorization Agreements Not Required

Under this agreement, individual IAAs will not be required for studies reviewed by either the Emory or the Georgia Tech IRB. Investigators must inform both IRBs when they plan to invoke the IAA already established between Emory and Georgia Tech. For more information, contact the Georgia Tech Office of Research Integrity Assurance at irb@gatech.edu.

5. Conflicts of Interest

Each institution will review its research for Financial Conflicts of Interest (COI) in compliance with applicable laws and regulations and its own published policies and procedures. The Relying Institution shall provide documentation of the review and any resulting management plan to the Reviewing Institution. The Reviewing IRB will have the authority to impose additional prohibitions or conflict management requirements necessary for the Reviewing IRB to approve the research protocol.

B. St. Joseph's Hospital, Inc. and Georgia Institute of Technology Reciprocal Agreement

St. Joseph's Hospital and Georgia Tech have entered into an Interinstitutional Authorization Agreement (IAA) setting forth the terms and conditions under which each entity may rely on the other for IRB review.

If a PI or co-investigator on a protocol has Georgia Tech as a home institution, but the protocol activities (excluding data analysis) take place at a Saint Joseph's Hospital site, then the Saint Joseph's Hospital IRB will serve as the reviewing institution for primary review and oversight of the protocol.

If a PI or co-investigator on a protocol has Saint Joseph's Hospital as a home institution, but the protocol activities (excluding data analysis) take place at a Georgia Tech site, then the Georgia Tech IRB will serve as the reviewing institution for review and oversight of the protocol.

If the PI on a protocol has either Saint Joseph's Hospital or Georgia Tech as a home institution, and the protocol activities (excluding data analysis) take place at both Saint Joseph's Hospital and Georgia Tech sites, then both the Saint Joseph's Hospital IRB and the Georgia Tech IRB shall be responsible for review and oversight of the protocol.

1. Protected Health Information

Principal Investigators must obtain written authorization from research participants, or obtain a waiver of authorization from the appropriate IRB, to have full access to and use of patient health information, including, but not limited to, the Health Insurance Portability and Accountability Act of 1996 ("HIPAA") and its implementing regulations (45CFR.160 and .164).

There are other substantial requirements for the protection of PHI under this agreement with St. Joseph's Hospital. Any Georgia Tech investigator proposing to obtain PHI under this agreement must confer with the Office of Research Integrity Assurance during protocol review.

2. Individual Interinstitutional Authorization Agreements Not Required

Under this agreement, individual IAAs will not be required for studies reviewed by either the St. Joseph's Hospital IRB or the Georgia Tech IRB. Investigators must inform both IRBs when they plan to invoke the IAA. For more information, contact the Georgia Tech Office of Research Integrity Assurance at irb@gatech.edu.

C. Consent Harmonization with Shepherd Center

Georgia Tech enjoys a collegial research partnership with the Shepherd Center. While the two entities have not agreed to defer IRB oversight to the other, both have informally agreed to harmonization of consent documents used in collaborative studies, as follows: Language must be the same in consent forms used by both entities. It is not necessary for both IRBs to date stamp approval periods on the documents.

D. Children's Hospital of Atlanta and Georgia Institute of Technology Authorization Agreement

Children's Healthcare of Atlanta (Children's) and the Georgia Institute of Technology have entered into an Interinstitutional Authorization Agreement setting forth the terms and conditions under which each entity may rely on the other for IRB review. Both entities have agreed that if a protocol provides for more of the protocol activities to take place at Children's than at Georgia Tech, then the Georgia Tech IRB shall be the relying IRB and shall rely upon the Children's IRB for review and oversight of the protocol. Conversely, if the protocol provides for more of the protocol activities to take place at a Georgia Tech site than at a Children's site, then the Children's IRB shall be the relying IRB and shall rely upon the Georgia Tech IRB for review and oversight of the protocol.

The foregoing notwithstanding, each Institution reserves the right at any time to assert its jurisdiction over the review of a protocol and to require its concurrent review of the protocol but must do so in writing to the PI and to the other institution's IRB.

Each of the Institutions and their respective IRBs shall comply, and shall require any persons or entities performing the Protocol on the respective parties behalf to comply, with all applicable federal and state laws and regulations governing the privacy and confidentiality of patient health information, including, but not limited to, HIPAA. Each of the Institutions and their respective IRBs shall take all actions necessary to comply with such laws and regulations, including amending this Agreement as required for

compliance. Each Institution's IRB shall require the Principal Investigator to obtain written authorization from the Protocol participants, or obtain a waiver of authorization from its IRB, or take such other actions required to permit the research sponsor, its employees, agents or affiliates, both IRBs and the Institutions, relevant regulatory agencies, other research sites involved in the Protocol, health care providers who may provide treatment or other services to Protocol participants, and laboratories or other individuals or entities that may analyze Protocol participants' "protected health information" as defined under HIPAA ("PHI") in connection with the Protocol to have full access to and use of Protocol participants' information. Each party and their respective IRBs shall limit its use and/or disclosure of and to require that its agents and subcontractors limit their use and/or disclosure of PHI, as permitted or required by this Agreement, the HIPAA authorization, the informed consent or as otherwise required by law. Each party and their respective IRB shall use commercially reasonable efforts to maintain the security of PHI and to prevent the unauthorized use and/or disclosure of such PHI. Each Institution and their respective IRBs agree to report to the other Institution and in the case of Children's, Georgia Tech shall report to the Children's designated Privacy Officer, in writing, any use and/or disclosure of PHI that is not permitted or required by this Agreement of which that Institution becomes aware within thirty (30) days of the Institution's discovery of such unauthorized use and/or disclosure of such PHI.

E. The University of Georgia and Georgia Institute of Technology Reciprocal Agreement

The University of Georgia (UGA) and Georgia Tech have executed an Interinstitutional Authorization Agreement (IAA) setting forth the terms and conditions under which UGA and GT may rely on the other for IRB review.

1. Student Research

If a protocol is initiated by a UGA student who is working on the protocol with a PI whose Home Institution is Georgia Tech or by a UGA student wishes to join the research team on a protocol initiated by a PI whose Home Institution is Georgia Tech, and the majority of Protocol activities (excluding data analysis) are to be completed at an Georgia Tech sites, then the UGA IRB shall rely upon the Georgia Tech IRB for review and oversight of the Protocol.

If a protocol is initiated by a Georgia Tech student who is working on the Protocol with a PI whose Home Institution is UGA or by a Georgia Tech student who wishes to join the research team on a Protocol initiated by a PI whose Home Institution is UGA, and the protocol activities (excluding data analysis) are to be completed at UGA sites, then the Georgia Tech IRB shall rely upon the UGA IRB for review and oversight of the Protocol.

If a protocol is initiated by either a Georgia Tech or UGA student and the protocol activities (excluding data analysis) take place both at UGA and Georgia Tech sites, then the IRB Directors or their designees from each institution shall jointly determine which IRB shall be responsible for review and oversight of the protocol.

2. Faculty/Staff Research

If a PI or co-investigator on a Protocol has Georgia Tech as a Home Institution, but the majority of Protocol activities (excluding data analysis) take place at UGA sites, then the Georgia Tech IRB shall rely upon the UGA IRB for review and oversight of the Protocol.

If a PI or co-investigator on a Protocol has UGA as a Home Institution, but the Protocol activities (excluding data analysis) take place entirely at Georgia Tech sites, then the UGA IRB shall rely upon the Georgia Tech IRB for review and oversight of the Protocol.

If the PI on a Protocol has either UGA or Georgia Tech as a Home Institution, and the Protocol activities (excluding data analysis) take place at both UGA and Georgia Tech Sites, then the IRB Directors or their designees from each institution shall jointly determine which IRB shall be responsible for review and oversight of the protocol.

3. Protected Health Information

In accordance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and notwithstanding anything to the contrary above, if the protocol activities (including data analysis) involve the use and/or disclosure of Protected Health Information as defined by HIPAA, then the Reviewing IRB will act as privacy board with respect to the Protocol in addition to its other review and oversight responsibilities regarding the Protocol.

D. Reliance by the Georgia Tech IRB upon the IRB at Another Institution

On occasion, the Georgia Tech IRB will rely upon the Institutional Review Board for approval and oversight of a research activity involving human subjects. Such reliance requires that the reviewing IRB shall hold a currently approved Federalwide Assurance, and an Interinstitutional Authorization Agreement (IAA) shall be drawn to document the terms and conditions under which the Georgia Tech IRB shall rely on the other.

In such cases, the Georgia Tech Principal Investigator should create a new protocol in IRBWISE and upload all documents associated with the study. This

will include copies of the approved protocol and consent documents, and the other IRB's letter of approval. The IRBWISE protocol title should begin with the name of the other institution, ie: "Great Western University: Name of Study." The new protocol must be submitted to the Georgia Tech Office of Research Integrity Assurance, not for Georgia Tech IRB approval, but in order to document the reliance upon "Great Western University" and that IRB's approval.

XXV. Research by Non-Georgia Tech Personnel or Entities Enrolling Georgia Tech Faculty, Staff, or Students

Reviewed: July 2024

Occasionally, non-Georgia Tech personnel or other entities will collect data from faculty, staff, and/or students on campus. The determination as to whether the Georgia Tech IRB needs to review the proposed activity depends on whether Georgia Tech is *engaged* in the research.

A. Georgia Tech *Is* Engaged in the Research

If Georgia Tech is engaged in the study, IRB review is required. An institution is considered *engaged* [as defined in §45CFR46.101 in non-exempt human subjects research when the involvement of their employees or agents in that project includes any of the following:

- Institutions that receive an award through a grant, contract, or cooperative agreement directly from HHS for the non-exempt human subjects research (i.e. awardee institutions), even where all activities involving human subjects are carried out by employees or agents of another institution.
- Institutions whose employees or agents intervene *for research purposes* with any human subjects of the research by performing invasive or noninvasive procedures. Examples include drawing blood; collecting buccal mucosa cells using a cotton swab; administering individual or group counseling or psychotherapy; administering drugs or other treatments; surgically implanting medical devices; utilizing physical sensors; and utilizing other measurement procedures.
- Institutions whose employees or agents intervene *for research purposes* with any human subject of the research by manipulating the environment. Examples of manipulating the environment include controlling environmental light, sound, or temperature; presenting sensory stimuli; and orchestrating environmental events or social interactions.
- Institutions whose employees or agents interact *for research purposes* with any human subject of the research. Examples of interacting include engaging in protocol-dictated communication or interpersonal contact, asking someone to provide a specimen by voiding or spitting into a

specimen container, and conducting research interviews or administering questionnaires.

- Institutions whose employees or agents obtain the informed consent of human subjects for the research.
- Institutions whose employees or agents obtain *for research purposes* identifiable private information or identifiable biological specimens from any source for the research. It is important to note that, in general, institutions whose employees or agents obtain identifiable private information or identifiable specimens for non-exempt human subjects research are considered engaged in the research, even if the institution's employees or agents do not directly interact or intervene with human subjects. In general, obtaining identifiable private information or identifiable specimens includes, but is not limited observing or recording private behavior; using, studying, or analyzing *for research purposes* identifiable private information or identifiable specimens provided by another institution; and using, studying, or analyzing *for research purposes* identifiable private information or identifiable specimens already in the possession of the investigators. In general, private information or specimens are considered individually identifiable [as defined in §45CFR46.102(e)] when they can be linked to specific individuals by the investigator either directly or indirectly through coding systems.

B. Georgia Tech *Is Not* Engaged in the Research

In those cases where Georgia Tech is not engaged in the research, review by the Georgia Tech IRB is not required. For example, marketing research firms may send email to Georgia Tech students, inquiring about their vacation preferences. If the email addresses are not provided by any Georgia Tech office, and if there are no Georgia Tech-associated research personnel, the IRB will not review the study.

In cases where Georgia Tech faculty, staff, or students are conducting human subjects research at Georgia Tech *strictly in their capacity as students at another institution*, they must obtain IRB approval from the institution where they have matriculated but the Georgia Tech IRB will not review the study.

Georgia Tech would not be considered engaged in research when Georgia Tech employees:

- inform prospective subjects about the availability of the research;
- provide prospective subjects with information about the research (which may include a copy of the relevant informed consent document and other IRB approved materials) but do not obtain subjects' consent for the research or act as representatives of the investigators;

- provide prospective subjects with information about contacting investigators for information or enrollment;
- seek or obtain the prospective subjects' permission for investigators to contact them; and/or
- permit use of Georgia Tech facilities for intervention or interaction with subjects by investigators from another institution.

Examples of non-engagement in the research:

An example of this would be a clinician who provides patients with literature about a research study at another institution, including a copy of the informed consent document, and obtains permission from the patient to provide the patient's name and telephone number to investigators.

Examples would be a school that permits investigators from another institution to conduct or distribute a research survey in the classroom; or a business that permits investigators from another institution to recruit research subjects or to draw a blood sample at the work site for research purposes.

XXVI. Non-Georgia Tech Personnel (including Visiting Scholars and Minors) Participating in Conduct of Protocols at Georgia Tech

Reviewed: July 2024

Georgia Tech celebrates and fosters collaborative relationships with non-Georgia Tech researchers and scientists who visit the Institute and who may wish to participate as researchers in projects at Georgia Tech. In order to ensure appropriate protections for those visitors and for Georgia Tech faculty and staff, this policy has been developed:

Any visiting non-Georgia Tech personnel wishing to participate as a researcher on a study involving human subjects must complete a VISITING SCHOLAR AGREEMENT with the associated academic department's HR representative, and must either be named in the original protocol application or be added by amendment to an existing protocol prior to participation in the protocol.

The Visiting Scholar's current CV or completed credentials form must be submitted to the Office of Research Integrity Assurance, and the Visiting Scholar must either complete the GT-required CITI training modules or present documentation of completion of another acceptable course. Upon approval by the IRB, such Visiting Scholars may serve as co-investigators working with Georgia Tech Principal Investigators who are responsible for conducting the research and ensuring compliance with the approved protocol.

The Georgia Institute of Technology has set forth specific eligibility requirements for the title of Principal Investigator (PI). These requirements apply not only in regard to IRB protocols, but also for protocols involving vertebrate animals or rDNA, and for serving as a PI on a sponsored project.

A. Participation of Minors as Employees or Volunteers in Laboratory and Other Activities Related to Human Subjects Research

Occasionally, minors, ages 16 or 17, will work in laboratories and other research environments at Georgia Tech. Some minors are employed as Tech Temps, while others are volunteers. These scholarly activities are enriching and often cement minors' interest in pursuing higher education in science, technology, engineering and mathematics (STEM) fields.

Georgia Tech's Office of Human Resources can provide guidance to departments hiring minors, including requirements of the Board of Regents (BOR) of the University System of Georgia that must be followed. The BOR requirements are set forth in their Human Resources Administrative Practice Manual which is posted online at https://www.usg.edu/hr/manual. Some of the requirements are:

- Each institution may allow departments to hire persons age sixteen and seventeen into temporary positions during recognized school breaks under certain conditions.
- If the minor is to work or volunteer in a laboratory setting or other hazardous area, the Supervising Faculty Member and/or Mentor must contact Georgia Tech's Office of Environmental Health and Safety and complete an *"Application for Authorization of a Minor (16 or 17 years of age) to Work or Volunteer in a Laboratory or other Hazardous Area."* This authorization must occur prior to the start date.
- The parent/legal guardian of the minor must also complete the *"Consent for Minor's Presence in Laboratory" form* and return it to Georgia Tech's Office of Environmental Health and Safety. Execution of this form is important, and it must be accomplished prior to the minor beginning to work or volunteer.
- Minors who are volunteers must provide evidence of personal health insurance as the Minor is responsible for their own medical care and all associated costs.
    - The department hosting the volunteer should retain the insurance information and all other necessary documentation for hosting the volunteer. Releases should be obtained and/or Risk Management should confirm that there is a recognized volunteer program for insurance coverage.
    - The department must also ensure compliance with the Georgia Tech Child Abuse Prevention policy, which is posted online at http://www.policylibrary.gatech.edu/mandatory-reporting-child-abuse-policy.

- The BOR requires that the supervising faculty member or mentor shall have constant line-of-sight supervision of the Minor at all times *while in the laboratory.*

XXVII. Investigator's Responsibilities When Conducting Research Activities Subject to DHHS

Revised: July 2024

Investigators who involve human subjects in their research have several specific responsibilities, some institutional, some regulatory, as indicated below:

A. Investigator Responsibilities Required by Georgia Institute of Technology Institutional Review Board

All investigators at Georgia Tech must comply with these *Policies & Procedures* when conducting research involving human subjects.
Investigators must:

1. Obtain approval from the Georgia Tech Institutional Review Board before undertaking research with human subjects.
2. Receive a written letter of approval from the Office of Research Integrity Assurance to document that IRB review occurred and approval was given. (Such letters of approval are frequently required by the funding sponsor and by publishers prior to publication in refereed journals).
3. Conduct every aspect of the project as approved by the Georgia Tech IRB.
4. Seek IRB review and approval by prior to revising the protocol. (The only exception to this policy is in situations where changes in protocol are required to eliminate apparent, immediate hazards to subjects).
5. Promptly report any unanticipated problems involving risks to subjects or others.
6. Assume full responsibility for selecting subjects in strict accordance with the inclusion/exclusion criteria outlined in the application materials.
7. Use only IRB-approved consent language. Approved consent documents are date-stamped by Research Integrity. While there is no federal requirement that consent documents must be date-stamped, the specific *approved* language must be used in the consent process.
8. Comply with the applicable DHHS and FDA regulations, including the investigator responsibilities specified by both agencies.

B. Investigator Responsibilities Required by DHHS Regulations at §45CFR46

1. IRB Review and Approval

Investigators are responsible for obtaining IRB approval before beginning any human subjects research (§45CFR46.109). Investigators are responsible for providing the IRB with sufficient information and related materials about the research (e.g., grant applications, research protocols, sample consent documents) so that the IRB can fulfill its regulatory obligations, including making the required determinations under §45CFR46.111 and, if applicable, subparts B, C and D. Investigators should follow institutional policies and procedures for IRB review that are required by HHS regulations at §45CFR46.103.

Investigators play a crucial role in protecting the rights and welfare of human subjects and are responsible for carrying out sound ethical research consistent with research plans approved by an IRB. Along with meeting the specific requirements of a particular research study, investigators are responsible for ongoing requirements in the conduct of approved research that include, in summary:

2. Informed Consent

Investigators are responsible for obtaining and documenting the informed consent of research subjects or their legally authorized representatives, unless the IRB approves a waiver of informed consent, or a waiver of documentation of informed consent, respectively (§45CFR46.116, §45CFR46.117). Investigators must give a copy of the informed consent document to each research subject (or the subject's legally authorized representative), and keep the signed original or a copy of it for their records (§45CFR46.117(a); §45CFR46.115(b)). When the documentation requirement is waived, the IRB may require investigators to provide subjects with a written statement regarding the research (§45CFR46.117(c)).

3. Amendments

Investigators are responsible for obtaining prior approval from the IRB for any modifications of the previously approved research, including modifications to the informed consent process and document, except those necessary to eliminate apparent immediate hazards to subjects (§45CFR46.103). If investigators wish to modify an ongoing IRB-approved research study, they must submit a request to the IRB and receive IRB approval before implementing the proposed modification,

unless the change is designed to eliminate an apparent immediate hazard to subjects (§45CFR46.103). If the investigators change the research in order to eliminate apparent immediate hazards to subjects without prior IRB approval, they should report those changes promptly to the IRB. The HHS protection of human subjects regulations allow for expedited review and approval of requests for minor changes in previously approved studies (§45CFR46.110(b)(1)).

4. Amendments that Render Exempt Research Nonexempt

Investigators should consult with the appropriate institutional authority whenever questions arise about whether planned changes to an exempt study [defined at §45CFR46.104(d)] might make that study nonexempt human subjects research. The designated entity at Georgia Tech for making a determination of exemption is the Institutional Review Board. If a determination of exemption is made by an authorized member of the IRB, the Office of Research Integrity Assurance will issue a letter of exemption. *Investigators at Georgia Tech do not have the authority to make an independent determination that human subjects research is exempt.*

5. Progress Reports and Continuing Review

Continuing review of minimal risk research is not required, unless otherwise determined by the IRB (§45CFR46.109(f)(1)). If research is determined and justified to require continuing review, investigators are responsible for ensuring that progress reports and requests for continuing review and approval are submitted to the IRB in accordance with the policies, procedures, and actions of the IRB as referenced in the institution's OHRP-approved Federalwide assurance (§45CFR46.108(a)(3), (45CFR46.109(e).

Investigators are responsible for fulfilling requirements associated with continuing review in time for the IRB to carry out review prior to the expiration date of the current IRB approval. Investigators are responsible for submitting all required materials and information for the IRB to meet its regulatory obligations, and should follow the institutional policies and procedures for continuing IRB review of research that are required by HHS regulations at §45CFR46.103 and referenced in the institution's OHRP-approved Federalwide assurance.

If IRB approval of a specific study expires before continuing review and approval occur, investigators must stop all research activities involving human subjects related to that study (§45CFR46.103), except where they judge that it is in the best interests of already enrolled subjects to continue to participate. When investigators make this judgment, they

must promptly notify the IRB (§45CFR46.103). When the IRB reviews the investigator's decision, it may decide whether it is in the best interests of already enrolled subjects to continue to participate in the research by considering the best interests of subjects either one at a time or as a group. If an IRB determines that it is not in the best interests of already enrolled subjects to continue to participate, investigators must stop all human subjects research activities, including intervening or interacting with subjects, or obtaining or analyzing identifiable private information about human subjects (§45CFR46.103). Investigators may resume the human subjects research activity once continuing review and approval by the IRB has occurred.

6. Records the Investigator Must Keep

The HHS protection of human subjects regulations require institutions to retain records of IRB activities and certain other records frequently held by investigators for at least three years after completion of the research (§45CFR46.115(b)).

Documentation of the informed consent of the subjects - either the signed informed consent form or the short form and the written research summary - are records related to conducted research [§45CFR46.115(b)] that *must be retained by investigators for at least three years after completion of the research*, unless the IRB waived the requirement for informed consent or for documentation of informed consent (§45CFR46.117).

Investigators must retain the records in hardcopy, electronic or other media form accessible for inspection and copying by authorized representatives of HHS at reasonable times and in a reasonable manner (§45CFR46.115(b)). Retention of multiple copies of each record is not required. Investigators should follow the institution's *Policies & Procedures* for retaining records. If investigators who have been designated to retain records on behalf of the institution leave that institution, the investigators and the institution should identify the successor responsible for maintaining those institutional records, either at the original institution or wherever the records are relocated, for the period of time required under HHS regulations at §45CFR46.115(b). Other regulations or policies may apply to the retention of records, including study data.

7. Additional DHHS Regulatory Requirements

In certain circumstances, investigators are responsible for meeting the following additional regulatory requirements:

- providing to the IRB prompt reports of any unanticipated problems involving risks to subjects or others §45CFR46.103;
- providing to the IRB prompt reports of serious or continuing non-compliance with the regulations or the requirements or determinations of the IRB (§45CFR46.103);

C. Conflict of Interest

A conflict of interest occurs when there is a divergence between an individual's private interests and their professional obligations to the Institute, such that an independent observer might reasonably question whether the individual's professional actions or decisions are influenced by considerations of personal gain, financial or otherwise. A conflict of interest depends on the situation, and not on the character or actions of the individual.

Conflicts of interest are common and practically unavoidable in a modern research university. At the Georgia Institute of Technology, conflicts of interest can arise out of the fact that a mission of the Institute is to promote public good by fostering the transfer of knowledge gained through Institute research and scholarship to the private sector. Two important means of accomplishing this mission include faculty consulting and the commercialization of technologies derived from faculty research. It is appropriate that faculty be rewarded for their participation in these activities through consulting fees and sharing in royalties resulting from the commercialization of their work. These rewards may be misunderstood or misconstrued and must therefore be carefully managed and appropriately disclosed.

Investigators who have a substantial financial interest in the outcome of the research, and those whose family members have a substantial financial interest in the outcome of the research, must, during the consent process, disclose the conflict to potential subjects. This includes providing a written disclosure on the consent form to explain and document the disclosure.

An appropriately managed conflict that is fully disclosed to participants does not always negatively affect recruitment. Appropriately managed conflicts are registered with Georgia Tech's Office of General Counsel, and approved plans for management are to be on record with that office. Questions should be forwarded to the Office of General Counsel.

There will be cases in which the Georgia Institute of Technology has a financial interest in the research project, and in those cases, disclosure must likewise be made and documented during the consent process.

Finally, no investigator who is a member of the reviewing IRB participates in the review of any study on which that member has a potential conflict of interest or is named on the research team.

XXVIII. Amendments and Other Proposed Changes

Revised: July 2024

A. Amendments and Other Proposed Changes

All *amendments* to protocols must be approved by the IRB before implementation of the revised study or use of a revised consent/permission/assent form. *All proposed changes* to procedures, recruitment, risk/benefit, personnel on the research team, funding sources, and any other aspect of the study are to be submitted to the IRB for review via IRBWISE *prior to their implementation.*

In accord with §21CFR56.110(b), the IRB utilizes expedited review procedures to review minor changes in ongoing previously-approved research during the period for which approval is authorized. An expedited review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB.

When a proposed change in a research study is not minor (e.g., procedures involving increased risk or discomfort are to be added), then the IRB must review and approve the proposed change at a convened meeting before the change can be implemented. The only exception is a change necessary to eliminate apparent immediate hazards to the research subjects [§21CFR56.108(a)(4)]. In such a case, the change must be reported to the IRB promptly. The IRB will then review the change to determine that it is consistent with ensuring the subjects' continued welfare.

1. Consent Addendum

Changes to consent/permission/assent forms may be required as a result of an amended protocol, or subsequent to review of adverse events (i.e., addition to the risks section of the consent form). The revised version should be used to consent new subjects for enrollment in the study. *However, in order to inform subjects who are already enrolled in the study of the changes to the study, the following format should be used.* If the study involves minors, an additional addendum, directed to the parent(s), and a revised assent form should be drafted as well. A sample follows.

Georgia Institute of Technology
Addendum to Consent Form
Project Title: XXXXXXXXXXXXXXXXX
Investigators:XXXXXXXX

You have already agreed to be a volunteer in the research study referenced above. The consent form that you signed (attached) stated that you would be told of any new information that might affect your willingness to continue in this study.

This addendum serves to tell you that …*(e.g., your participation will be extended another 3 weeks….OR…An additional 3 tsp. of blood will be taken at your 4th visit…. …etc.).*

(If applicable, explain why the change is being implemented, and provide details regarding relevant changes to risks, benefits, etc. that occur as a result of the revised protocol.)

You are reminded that:

- All other information from the original consent form remains unchanged,
- Your participation in this study continues to be voluntary. You do not have to be in this study if you don't want to be.
- You have the right to change your mind and leave the study at any time without giving any reason, and without penalty.
- Any new information that may make you change your mind about being in this study will be given to you.
- You will be given a copy of this consent addendum to keep.
- You do not waive any of your legal rights by signing this consent form.

If you have any questions about the study, you may contact [Dr. P. Investigator], at telephone (XXX) XXX-XXXX.

If you have any questions about your rights as a research subject, you may contact:

Research Associate for the PI's department
Office of Research Integrity Assurance
Georgia Institute of Technology
irb@gatech.edu

If you sign below, it means that you have read (or have had read to you) the information given in this consent form addendum, and you would like to continue to be a volunteer in this study.

_____
Subject Name

_____ _____

XXIX. Protocol Deviations, Violations, and Exceptions

Reviewed: July 2024

A protocol deviation or violation is defined as any change to, or departure from, the approved protocol that is not approved by the IRB prior to its initiation or implementation, OR any deviation from standard operating procedures, Good Clinical Practices (GCPs), federal regulations, or institute policies. The PI must report a major protocol deviation or violation to the Office of Research Integrity Assurance as soon as possible after becoming aware that it occurred, but always within seven days of its occurrence.

A. Major Protocol Deviations and Violations

Deviations and violations meeting any of the following criteria are considered major:

- A *serious failure* by the study team to comply with the protocol, standard operating procedures, good clinical practices, or with federal, state or local regulations. Such deviations or violations may not be intentional. (*Serious failure is non-compliance that adversely affects the rights and welfare of subjects or places them at increased risk of harm*).
- *Continuing failure* of the study team to comply with the protocol, standard operating procedures, good clinical practices, or with federal, state or local regulations. Such deviations or violations may not be intentional. (*Continuing failure is a pattern of non-compliance that is willful or that indicates a lack of knowledge that may increase the likelihood of an adverse effect on the rights and welfare of subjects or may place them at an increased risk of harm.)*
- Subject safety or risk/benefit ratio is impacted by the deviation or violation, even if actual harm does not result.
- The deviation or violation significantly damages the completeness, accuracy and reliability of the data collected;

Regardless of their potential impact on subject safety or on the risk/benefit ratio of the protocol, these are considered major protocol deviations or violations and require immediate reporting to the Office of Research Integrity Assurance:

- Consenting not done in conformance with the approved plan (subjects not consented, or consented after study began);
- Inclusion or exclusion criteria not followed;

- Dosing errors.

B. Minor Protocol Deviations

Minor protocol deviations and violations are just that—minor. They do not constitute a serious failure to comply with the protocol, standard operating procedures, good clinical practices, or with federal, state or local regulations. Minor protocol deviations and violations do not constitute a continuing failure to comply, nor do they impact subject safety or substantively alter the risk/benefit ratio. Subject safety or risk/benefit ratio is not impacted by the deviation or violation, and the minor deviation or violation does not significantly damage the completeness, accuracy and reliability of the data collected.

Minor deviations and violations must be reported to the Office of Research Integrity Assurance within 30 days of their occurrence.

C. Protocol Exceptions

A *protocol exception* differs from an amendment in that an exception involves a single subject (or, very rarely, a small number of subjects) and does not constitute failure to comply with the approved protocol. An exception is not a permanent change to the research protocol and must be approved by the IRB prior to implementation. Exceptions generally involve the enrollment of a subject who does not meet the approved inclusion criteria. Enrollment of such subjects requires justification, including convincing evidence that participation is in the best interest of that subject.

If the study involves an investigational drug, device, or biologic, prior approval by the sponsor is also required. If the research involves an investigational device *and* the exception may affect the scientific soundness of the research plan or the rights, safety, or welfare of the subjects, Food and Drug Administration (FDA) pre-approval is required [§21CFR812.150(4)].

The PI is responsible for obtaining prior approval from the IRB for exceptions. Protocol exceptions may be submitted online via IRBWISE and, if applicable, documentation of sponsor and FDA approval must be uploaded with the exception request. If appropriate, information sheets for subjects and/or revised consent or informational scripts must be submitted.

XXX. Adverse Events and Unanticipated Problems

Reviewed: July 2024

Federal regulations at §21CFR56.108(b)(1) and at §45CFR46.103 require the IRB to follow written procedures for ensuring prompt reporting to the IRB of any unanticipated problems involving risk to human subjects or others.

Guidance from the Office for Human Research Participants (OHRP) states that, before research is approved and the first subject enrolled, the investigator(s) and the IRB should give appropriate consideration to the spectrum of adverse events that might occur in subjects. In particular, in order to make the determinations required for approval of research under HHS regulations at §45CFR46.111, the IRB needs to receive and review sufficient information regarding the risk profile of the proposed research study, including the type, probability, and expected level of severity of the adverse events that may be caused by the procedures involved in the research. The investigator also should describe how the risks of the research will be minimized.

A. Adverse Events

The FDA defines an adverse event as *any undesirable experience associated with the use of a medical product in a patient*. The HHS regulations at §45CFR46 do not define or use the term *adverse event*, nor is there a common definition of this term across government and non-government entities. The Office for Human Research Protections (OHRP) utilizes this definition: *An adverse event is "Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research (modified from the definition of adverse events in the 1996 International Conference on Harmonization E-6 Guidelines for Good Clinical Practice)."*

Adverse events encompass both physical and psychological harms. They occur most commonly in the context of biomedical research, but they can also occur in social and behavioral research.

An adverse event may be both serious and unanticipated.

1. Serious Adverse Events

A *serious adverse event* is one that is fatal, life-threatening, persistent, significantly disabling or incapacitating, requires inpatient hospitalization or prolongation of hospitalization, results in congenital anomaly or defect, and/or that is a significant medical incident. (A significant medical incident is considered a serious, study-related adverse event because it may jeopardize the subject's health and may require medical or surgical intervention to prevent a poor outcome.)

The FDA requires that serious events be reported when the patient outcome is:

- **Death**: Report if the patient's death is suspected as being a direct outcome of the adverse event.
- **Life-Threatening**: Report if the patient was at substantial risk of dying at the time of the adverse event or it is suspected that the use or continued use of the product would result in the patient's death. *Examples: Pacemaker failure; gastrointestinal hemorrhage; bone marrow suppression; infusion pump failure which permits uncontrolled free flow resulting in excessive drug dosing.*
- **Hospitalization (initial or prolonged)**: Report if admission to the hospital or prolongation of a hospital stay results because of the adverse event. *Examples: Anaphylaxis; pseudomembranous colitis; or bleeding causing or prolonging hospitalization.*
- **Disability**: Report if the adverse event resulted in a significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities or quality of life. *Examples: Cerebrovascular accident due to drug-induced hypercoagulability; toxicity; peripheral neuropathy.*
- **Congenital Anomaly**: Report if there are suspicions that exposure to a medical product prior to conception or during pregnancy resulted in an adverse outcome in the child. *Examples: Vaginal cancer in female offspring from diethylstilbestrol during pregnancy; malformation in the offspring caused by thalidomide.*
- **Requires Intervention to Prevent Permanent Impairment or Damage**: Report if you suspect that the use of a medical product may result in a condition which required medical or surgical intervention to preclude permanent impairment or damage to a patient. *Examples: Acetaminophen overdose-induced hepatotoxicity requiring treatment with acetylcysteine to prevent permanent damage; burns from radiation equipment requiring drug therapy; breakage of a screw requiring replacement of hardware to prevent malunion of a fractured long bone.*

2. Unanticipated Adverse Events

An *unanticipated adverse event* is one that results from a study intervention and was not expected or anticipated. Expected adverse events that occur with greater frequency or severity than expected may be characterized as unanticipated adverse events.

3. Unanticipated Adverse Device Effects (UADEs)

The Food & Drug Administration (FDA) investigational device exemption (IDE) regulations define an *unanticipated adverse device effect (UADE) as "any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects."* (§21CFR812.3(s))

4. When Adverse Events Must Be Reported

Investigators are required to *report to the Institutional Review Board within ten days of its occurrence* any serious problem, serious adverse event, or other outcome that occurs more frequently or with greater severity than anticipated. Further, if any event(s) cause the suspension, whether temporary or permanent, of a research study involving human subjects, the IRB must be informed within ten days. Such reports to the IRB must describe the adverse events' relevance and significance to the study and whether there is a change in the risk of participation.

When the GT PI is managing a study site on an NIH-supported multi-center clinical trial, in lieu of receiving individual adverse event reports from each of the clinical sites, the GT IRB should receive from the investigator a written summary report whenever a data safety monitoring board (DSMB) review has taken place.

Adverse events that are of minimal risk and anticipated (such as skin irritation from tape/sensors) may be reported at the next continuing review.

Adverse events are to be reported to the GT IRB via IRBWISE. Very serious and unanticipated events may be immediately reported by telephone to the Office of Research Integrity Assurance. Investigators are responsible for the accurate documentation, investigation and follow-up of all possible study-related adverse events.

a. PI-Initiated Studies
When the investigator is the study sponsor--that is, when the investigator is the holder of the Investigational New Drug (IND) or Investigational Device Exemption (IDE)—the investigator is responsible for reporting serious adverse events directly to the IRB and to the Food and Drug Administration (FDA). FDA requires use of the Form #3500a (Mandatory Medwatch Form).

b. Industry Sponsored Studies
When the study is industry-sponsored, the PI will also be required to report serious and unanticipated adverse events and problems to the sponsor, as well as to the GT IRB. This form may also be used to voluntarily report serious adverse events, potential and actual medical product errors, and product quality problems associated with the use of FDA-regulated drugs, biologics, devices and dietary supplements. Study sponsors may have different reporting processes.

Unanticipated Adverse Device Effects (UADEs) must be reported to the IRB and the sponsor within 10 working days after the investigator first learns of the effect (§812.150(a)(1)). Sponsors must immediately evaluate reports of an UADE and report the results to the FDA, all reviewing IRBs, and participating investigators within 10 working days after first receiving notice of the effect (§812.46(b), 812.150(b)(1)).

B. Unanticipated Problems Involving Risk to Subjects or Others (UPIRTSO)

An unanticipated problem is an event that was not anticipated or foreseen, involves risk to subjects or others and, in the judgment of the investigator, was related to or caused by the research activity. The loss of a laptop computer containing confidential information about subjects is an example of an unanticipated problem. In such cases, while subjects may not be physically harmed, the potential breach of confidentiality may cause them anxiety or embarrassment.

1. Requirement for Investigators to Report Unanticipated Problems

Serious unanticipated problems must be reported to the Office of Research Integrity Assurance by the Principal Investigator within ten working days of their occurrence. Very serious and unanticipated events may be immediately reported by telephone to the Office of Research Integrity Assurance at 404 / 385-2175 or 404 / 894-6942. Other unanticipated problems should be reported within thirty days. Any

protocol deviation to mitigate immediate risk or potential harm should also be reported. These reports may be submitted online via IRBWISE.

Such reports must include a complete description of what happened, when and where the event took place, and any resulting harm or injury to a subject or others. Principal Investigators must report to the Office of Research Integrity Assurance any injury to a human subject; unanticipated problems; new information that affects risk/benefit, and any evidence of research misconduct involving risks to research subjects. Reports of unanticipated problems should explain why the event represents a problem for the study and why it was unanticipated.

2. Requirement for Investigators to Monitor Problems

The Principal Investigator must monitor anticipated problems, subject complaints and any other issues that do not constitute an unanticipated problem requiring reporting to the IRB. These events should be recorded in a log maintained by the PI or research staff. The PI should consider whether such problems, complaints, or issues necessitate modification of the consent document or other protocol amendment.

C. Institutional Review Board Response to Reports of Adverse Events and Unanticipated Problems

Serious adverse events that occur on-site will be reviewed by the full committee at a convened meeting. Those occurring at another center conducting the study (i.e., in the case of multi-center studies) will be reviewed by the IRB in a timely manner.

The IRB may suspend or terminate approval of research at its site when there is unexpected serious harm to subjects. Such action shall be with the majority vote of IRB members at a convened meeting with a quorum. The Institutional Official will be immediately informed when the IRB makes such a determination. The Principal Investigator will also be immediately informed and will be provided a written statement of the action and the reasons for it. The IRB will also inform appropriate the Department or Agency head, the Office for Human Research Protections and the FDA, if an investigational new drug or device is involved. The IRB will communicate concerns to the Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC), if any, and/or to the sponsor of the study if it believes that the safety of study participants is in jeopardy.

The IRB Chair and the Institutional Official shall each have independent authority to suspend a study immediately when, in their judgment, human subjects are at risk of immediate harm. Such actions shall be reported to the

IRB at the next convened meeting, where the Board will determine whether such suspended study may continue.

These actions and IRB deliberations shall be documented in the meeting minutes and be retained in accordance with records requirements.

D. Incidental Findings

Incidental findings are possible medical abnormalities that may have clinical implications and are observed in the course of research studies but are unrelated to the topic under study. Examples might include:

- A study involving fractionation of normal human blood suggests a potential infection;
- A baseline study of mental status indicates a psychiatric condition;
- A screening protocol for an exercise intervention identifies a cardiac insufficiency;
- A brain imaging study of depressed individuals reveals a potential structural abnormality (From Nature, Vol. 433. January, 2005, p. 185.).

No National Institutes of Health (NIH) policies/guidance specifically address incidental findings, however, NINDS, NIDA, NIBIB, NIMH, NIA and Stanford University sponsored a meeting in 2005 on "Detection and Disclosure of Incidental Finding in Neuroimaging Research."

At this point, the NIH Office of Extramural Research (OER) suggests that investigators who propose studies that may result in incidental findings describe their plans for addressing incidental findings in the Human Subjects section of their applications as follows:

- how observed incidental findings will be handled by research staff, and
- how plans for handling incidental findings will be presented to potential participants during the informed consent process

The Georgia Tech IRB has written consent language, italicized below, that is required for MRI/fMRI studies conducted at the Center for Advanced Brain Imaging (CABI). Researchers may use this as a sample to develop similar language for other studies when appropriate.

"This MRI is done for research purposes only. The MRI scan being done is designed to answer research questions, not to medically examine your brain. The MRI scan is not a substitute for one a physician would order. It may not show problems that would be picked up by a medical MRI scan. None of the researchers are medically qualified radiologists. However, if we see something unusual in your scan, we will inform you so that you can obtain a follow-up evaluation by your physician. Any follow-up evaluation or treatment that you

seek will be at your own expense. Even if your physician rules out any problems, you may be unnecessarily worried if a problem is suspected."

Georgia Institute of Technology
Institutional Review Board
POLICIES AND PROCEDURES

XXXI. Institutional Review Board Responsibilities and Approval Processes

Reviewed: July 2024

In keeping with its charge to safeguard the rights and welfare of human participants in research, the Institutional Review Board has several specific responsibilities, and processes are in place to ensure that the IRB is in compliance with those requirements. Among the most important IRB responsibilities are initial protocol review, continuing protocol review, reporting findings & actions, determining review frequency, when to require outside verification of no changes since previous review, reporting proposed changes, and reporting unanticipated problems and continuing non-compliance to the Institutional Official, the Office for Human Research Protections, the Food and Drug Administration, National Institutes of Health, and so on. Those IRB processes are described here.

A. Initial Protocol Review

The Georgia Tech Institutional Review Board reviews protocols in accordance with the FDA and HHS requirements and as described in these policies. The components of a protocol application are described in section IX of these *Policies & Procedures*: "Procedures for Obtaining Institutional Review Board Approval."

The IRB has authority to approve, to require modifications in (to secure approval), or to disapprove all research activities covered by this policy. Research that has been approved by the Georgia Tech IRB may be subject to further appropriate review and approval by officials of the institution. However, those officials may not approve research if it has not been approved by the Georgia Tech IRB.

Protocols are submitted online via IRBWISE to the Office of Research Integrity Assurance. Research Associates log in the protocol, assign it a unique identifying number, and add the protocol to the agenda for the next convened meeting of the IRB. If the study qualifies for exempt or expedited review, a Research Associate or other member of the IRB conducts such review. Approvals of protocols, amendments, and/or continuing review applications must be given by a voting member of the IRB.

1. Requirements for Approval

In order to approve a research activity, the Georgia Tech IRB must determine that all of the following requirements are satisfied:

- No Georgia Tech IRB members will participate in the review of any study on which they are an investigator or co-investigator or where a potential for personal conflict of interest exists.
- Risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and, whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects and the importance of the knowledge that may reasonably be expected to result.
- Selection of subjects is equitable, in relation to the purposes of the research and the setting in which the research will be conducted.
- Informed consent is appropriately obtained. The IRB shall require that information given to subjects as part of informed consent is in accordance with §46.116. The IRB may require that information, in addition to that specifically mentioned in §46.116, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects. The IRB shall require documentation of informed consent or may waive documentation in accordance with §46.117. To ensure PI compliance with IRB policy regarding consent, the IRB may request a redacted copy of signed consent forms used to enroll subjects.
- An IRB shall notify investigators and the institution in writing of the outcome of the review, which may be to approve or disapprove the proposed research activity, or to require modifications to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.
- Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- Where some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as minors, persons with acute or severe physical or mental illness, or persons who are economically or educationally disadvantaged, appropriate

additional safeguards have been included in the study to protect the rights and welfare of these subjects.

2. Review for Scientific Merit

While federal regulations governing Institutional Review Boards do not clearly require IRB review of the scientific validity of an investigator's research design, the IRB determines whether risks to subjects are reasonable in relation to the importance of the knowledge that may reasonably be expected to result. The (then) Office for Protection from Research Risks issued guidance stating that *one of the ethical justifications for research involving human subjects is the social value of advancing scientific understanding and promoting human welfare by improving health care. But if a research study is so methodologically flawed that little or no reliable information will result, it is unethical to put subjects at risk or even to inconvenience them through participation in such a study"* (OPRR, 1993: 4-1).

With this guidance in mind, the Georgia Tech IRB generally leaves thorough scrutiny of the research design to the peer review process, if the project will receive funding from an external agency. The proposals of investigators not submitting to external agencies may be examined more closely for research design flaws and, depending on their seriousness, these flaws may need to be corrected before IRB approval is granted.

3. IRB Determination Regarding Risk

The IRB must determine that the following requirements are satisfied prior to issuing approval for proposed research involving human subjects.

a. Risks to subjects are minimized:
   (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
   (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

b. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies that subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge

gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

4. Determining Review Frequency

At the time of initial review, the IRB determines whether an independent data and safety monitoring board or committee is required, and also sets a date for reevaluating the research project. The IRB may determine that certain protocols necessitate review more frequently than every twelve months. Such protocols typically pose a higher risk of harm to subjects and/or involve a vulnerable population or very sensitive topic; these protocols generally undergo full board review. Concerns about the Principal Investigator's compliance can also prompt a requirement for more frequent review. The IRB shall determine at the time of review whether a shorter period of approval is appropriate, and the IRB will establish the required reporting schedule at approval. At its discretion, the IRB may require the investigator to report on progress at intervals of the board's choosing.

IRB approval periods are granted on the basis of degree of risk associated with the particular protocol, but never for a period longer than one year minus one day. During the course of a study, unexpected side effects may occur or knowledge resulting from another research project may become available. The IRB may then need to reassess the balance of risks to benefits. In light of the reassessment, the IRB may require that the research be modified or halted altogether. Alternatively, special precautions or criteria for inclusion may be relaxed. Between IRB reviews, it is largely the researchers' responsibility to keep the IRB informed of significant findings that affect the risk/benefit ratio. In larger studies or clinical trials, a data and safety monitoring committee may be responsible for keeping the IRB up-to-date. Even isolated incidents of unanticipated adverse reactions must be reported to the IRB. The IRB must then decide whether the research should be modified. In addition, a report from one research activity may sometimes be relevant to the evaluation of another. In such cases, the IRB may set an approval period of a few weeks or months, instead of one year minus one day.

5. Review Lead-Time Considerations

The length of time required for IRB review of a protocol is necessarily dependent on the review category. *Exempt* category projects are generally reviewed within 1-2 weeks of receipt date by the Research Associate. Protocols reviewed under expedited procedures are sent to board members on a regular basis. *Expedited* review is completed generally within three weeks of receipt date. Protocols requiring *full*

board review at a convened meeting of the IRB must be submitted by the deadline. Meeting dates and application deadlines are posted on the Office of Research Integrity Assurance website.

For protocols supporting a funded project, IRB materials should be submitted far enough in advance of the grant submission deadline to allow for two successive meetings of the IRB. Consultation with the Compliance Officer early in the planning stages is recommended in order to facilitate the coordination of the various deadlines to which the research activity may be subject for review. There are separate campus committees that are federally and/or state mandated to review research for compliance with regulations that govern involvement of, for example, animal subjects, recombinant DNA, and radioisotopes.

6. IRB Disapproval of Protocols

While all reviewers may exercise all authority of the IRB to review projects qualifying for expedited or exempt review, no individual member, including the Chair, may disapprove a research protocol. Any proposed disapproval is to be referred to the full board for review and disposition. Disapproval of a research protocol must be determined by a majority vote at a convened meeting of the full board where a quorum is present.

If the IRB does not approve a human subjects research activity, the board shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing. If the investigator is not satisfied with the decision to disapprove, the investigator may appeal. In such cases, the PI may meet with the board to discuss concerns, or the PI may request re-review after making changes to the research protocol or by providing significant new information.

7. Review by Institution

Research covered by this policy that has been approved by the IRB may be subject to further review and approval or disapproval by officials of the institution. However, those officials may not approve the research involving human subjects if it has not been approved by an IRB. *An IRB disapproval cannot be overruled by any institutional officer or official.*

B. Continuing Review Procedures

The federal regulations require continuing review only be required for studies that are more than minimal risk and those that the Institutional Review Board deems necessary. If the Institutional Review Board determines that a continuing review is necessary, the Institutional Review Board must then

justify this decision to the Office of Human Subjects Research Protections. When a continuing review is required, the Institutional Review Boards reevaluate research projects at intervals appropriate to the degree of risk but not less than once a year. Periodic review of the research activity is necessary to determine whether the risk/benefit ratio has shifted, whether there are unanticipated findings involving risks to subjects, and whether any new information regarding the risks and benefits should be provided to subjects. It is important to note that the risk/benefit ratio may change over time.

1. Automated Notification of Pending Expiration

Approximately 60 days prior to the end of the approval period, investigators will receive an automated email reminding them to submit continuation materials for the next approval period. A second automated email notice is sent about a month prior to expiration. The investigator is strongly urged to be aware of application deadlines and review lead-time considerations to ensure uninterrupted coverage of project approval. Continuations requiring full board review must be submitted with sufficient lead time. The current Georgia Tech IRB schedule of deadlines and meeting dates is available at https://oria.gatech.edu/irb.

2. Materials Required for Continuing Review

Progress Report: The progress report comprises a major portion of the continuation application. In IRBWise, the submission is considered the progress report. The progress report summarizes project activities over the past approval period; states number of subjects participating; describes adverse events, new information learned, results of research, and any publications. It further summarizes adverse events and unanticipated problems. In many cases, it is sufficient for the Principal Investigator to provide a brief statement that there have been no unanticipated problems and that adverse events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document, and any investigator brochure.

Consent/Permission/Assent form(s) to be used for the upcoming approval period. The Principal Investigator is to provide clean, unstamped copies of all consent documents to be utilized in the renewal period. Once reviewed and approved, the IRB will date-stamp these with the new approval period.

Study Documents: All study documents that are used during the course of the study to recruit, screen subjects, collect data, grant documents, etc. must be uploaded to the continuing review so that the documents can be reviewed and re-approved for the new approval period.

Signatures: The continuation application must be submitted through IRBWISE. As with original protocols, continuation applications must have the electronic signatures of the investigator, chair of the department or departmental review committee and, in the case of undergraduate or graduate student investigators, signature of the student's advisor or faculty member will be required.

3. Review Lead-Time Considerations

Continuing reviews are as rigorous as original protocol reviews, so investigators should plan on an equivalent amount of time to obtain continuing approval. As always, investigators are reminded to submit continuation materials well in advance of meeting dates when full board review is required.

4. Expiration of Approvals

When IRB approval expires, all activities involving human subjects must be stopped immediately, *including data analysis*, except in extraordinary cases involving an intervention that must continue for subject safety. Expired IRB protocols may only continue after the IRB reviews and approves a continuation application. If no continuation application is received within thirty days after expiration, the protocol will be closed by the Office of Research Integrity Assurance. The investigator will have to submit an entirely new protocol if the investigator wishes to take up that same work in the future.

5. Outside Verification That No Material Changes Have Occurred Since Previous Review

During the continuing review process, the Principal Investigator is asked to specify what changes, if any, have occurred since the previous IRB review. If deemed appropriate, the Office of Research Integrity Assurance and/or IRB members may perform a compliance audit to ascertain the degree of compliance.

6. Determining Which Studies Need Verification from Other Sources

The IRB generally relies on the Principal Investigator with an approved protocol to carry out the research as described to, and approved by, the IRB. Sometimes circumstances cause the IRB to require verification from sources other than the investigators regarding information related to the conduct of the study. Such circumstances might include an allegation of investigator misconduct, complaint from a subject, report filed by a third party whistleblower, a random compliance audit by the

Office of Research Integrity Assurance; or studies for which a Data Safety Monitoring Board has been established.

7. Ensuring that Changes in Approved Research Are Not Initiated without IRB Review and Approval

Investigators must obtain prior IRB approval for any changes in study procedures, except where necessary to eliminate immediate hazards to the participants. (If changes are implemented to eliminate hazards, the IRB must be notified no later than the next business day).

To ensure compliance, the Office of Research Integrity Assurance informs investigators of this requirement in written IRB approval letters. Investigators also are so informed during required training before they may initiate any study involving human subjects. The Office of Research Integrity Assurance may conduct random audits of investigator's study records to assess compliance.

8. Reporting IRB Findings and Actions to the Institutional Official

In cases where a previously approved research study is suspended or terminated by the IRB for reasons other than simple expiration of the approval period, the Institutional Official is notified by the Office of Research Integrity Assurance. Such terminations, suspensions, and other findings and actions are provided in writing to investigators and, in some cases, to their department heads and/or Deans.

9. Reporting Unanticipated Problems, Continuing Non-Compliance, Suspensions and Terminations to Oversight Agencies

Cases of serious or continuing non-compliance; unanticipated problems involving risks to participants or others; and suspension or termination of IRB approval must be reported to federal oversight agencies. The Office of Research Integrity Assurance prepares such written notification for submission by the Institutional Official to the Office for Human Research Protections, National Institutes of Health, the Food and Drug Administration, and/or the funding agency(ies), as appropriate.

C. Monitoring and Observation of Research by the IRB

The IRB has the authority to inspect records, and to observe (or have a third party observe) the consent process and any research activity that it approves (§45CFR46.109(g)). Depending upon the risks of the research and the likelihood that the research could involve risks to subjects that are unforeseeable, the IRB must ensure, if appropriate, that the research includes adequate provisions for monitoring the data collected to ensure the safety of

subjects (§45CFR46.111(a)(6)). Such provisions typically would include the following:

- The type of data or events that are to be captured under the monitoring provisions.
- The entity responsible for monitoring the data collected, including data related to unanticipated problems and adverse events, and their respective roles (e.g., the investigators, the research sponsor, a coordinating or statistical center, an independent medical monitor, a DSMB/DMC, and/or some other entity).
- The time frames for reporting adverse events and unanticipated problems to the monitoring entity.
- The frequency of assessments of data or events captured by the monitoring provisions.
- Definition of specific triggers or stopping rules that will dictate when some action is required.
- As appropriate, procedures for communicating to the IRB(s), the study sponsor, the investigator(s), and other appropriate officials the outcome of the reviews by the monitoring entity.
- Monitoring provisions should be tailored to the expected risks of the research; the type of subject population being studied; and the nature, size (in terms of projected subject enrollment and the number of institutions enrolling subjects), and complexity of the research protocol.

XXXII. Non-Compliance

Reviewed: July 2024

Non-compliance is generally defined as a serious and/or continuing failure by the Principal Investigator or research team to comply with the approved protocol, standard operating procedures, good clinical practices, with federal, state or local regulations, or with Institute policy, including these *Policies & Procedures*. Such violations may or may not be intentional.

A. Responsibility for Proper Conduct of Research Studies Involving Human Subjects

The ultimate responsibility for the conduct of a research project involving human subjects belongs to the Principal Investigator (PI). The Principal Investigator and all other members of the research team must comply with these *Policies & Procedures* and with appropriate federal regulations governing human subjects' protections and with the Georgia Institute of Technology's Federalwide Assurance. Research projects must be conducted in accordance with protocols as approved by the Institutional Review Board (IRB) and as outlined in these *Policies & Procedures*.

B. Allegations of Non-compliance

Allegations of non-compliance in a human subjects study should be brought to the attention of the IRB Chair, the Office of Research Integrity Assurance, or the Institutional Official. If an alleged non-compliance has caused, or may cause, injury or any other risks to subjects or others, the study shall be immediately suspended at the direction of the Institutional Official, and an inquiry and review by the full IRB or a subset of the IRB shall be ordered.

C. Full Board Review of Allegations of Non-compliance

In the event that a review of non-compliance by the full IRB is warranted, the Office of Research Integrity Assurance and Chair of the IRB shall notify the IRB and appoint a subcommittee of IRB members to conduct an investigation which will focus on the protection of study subjects. The Institutional Official will be kept informed and may participate in the investigation.

D. IRB Procedures for Resolution of Alleged Non-Compliance

The following points outline the procedures for resolving alleged non-compliance:

1. When a potential non-compliance is reported, the Office of Research Integrity Assurance will compile appropriate information from the complainant, the protocol file and other sources, and present concerns to the IRB Chair and the Institutional Official.
2. The IRB Chair or Director of Research Integrity Assurance will contact the Principal Investigator for the purpose of fact-finding, to determine whether the alleged non-compliance is intentional, unintentional, or the result of mistake or oversight.
3. If the initial discussion does not result in resolution of the matter, the allegation will be presented at the next IRB meeting by the IRB Chair or Office of Research Integrity Assurance.
4. An audit of study records may be called by the IRB or Institutional Official. Such audit shall be conducted by an audit team appointed by the IRB Chair, and shall include a subset of IRB members and at least one Research Associate.

In order to make a finding of non-compliance, the IRB must determine that:

1. There were violations of these institutional *Policies & Procedures*, the state and/or federal laws or regulations governing research with human subjects, good clinical practices, or Institute policy; and/or
2. There was a material failure to follow the approved protocol; and/or
3. The alleged non-compliance resulted in otherwise unanticipated problems involving risks to subjects.

If any of these are confirmed either through discussions with the investigator or by audit finding, the IRB must then determine whether the non-compliance is serious or continuing. A *serious compliance failure* may adversely affect the rights and welfare of subjects or places them at increased risk of harm. *Continuing failure* is a pattern of non-compliance that is willful or that indicates a lack of knowledge that may increase the likelihood of an adverse effect on the rights and welfare of subjects or may place them at an increased risk of harm.

In the event that non-compliance results from administrative oversight that is self-reported by the PI or other individual, the Office of Research Integrity Assurance shall compile the appropriate information and present the concerns to the IRB Chair and the Institutional Official. The Office of Research Integrity Assurance will work with the reporting party to correct the non-compliance.

E. Possible Outcomes of Non-compliance Inquiries and Investigations

Serious or continuing failure to comply with these requirements may result in study suspension and, in egregious cases, study termination, return of sponsor funding and the matter being reported to federal agencies and the sponsor.

Investigators may also be required by the Institutional Review Board to destroy data.

The Principal Investigator is provided written notification of determinations made, with copies to the departmental Chair or Dean, the Institutional Official, the Executive Vice President for Research, and others as appropriate. Should protocol suspension or termination result, the Office of Sponsored Programs will be notified in cases where there is external funding. The Office of Research Integrity Assurance, in collaboration with the Institutional Official, shall determine whether notification of federal regulatory agencies is also warranted.

Should there be an appearance of research misconduct, the Institute's procedures governing research misconduct will be implemented. Inquiries or investigations into research misconduct do not preclude IRB review and actions.

Confidentiality will be strictly observed during any inquiry and investigation, and due process for the Principal Investigator and members of the research team will be ensured.

F. Guidance on Reporting Incidents (non-compliance) to the Office for Human Research Protections

June 20, 2011 THIS GUIDANCE REPLACES OHRP'S MAY 27, 2005 GUIDANCE ENTITLED "GUIDANCE ON REPORTING INCIDENTS TO OHRP" This guidance has been updated to clarify what information regarding serious or continuing noncompliance by the institutional review board needs to be reported, to include an e-mail address to report incidents to OHRP, and to update OHRP's contact information.

1. Scope:

This document provides guidance about procedures institutions may use to file incident reports with OHRP. Incident reports include reports of unanticipated problems involving risks to subjects or others; serious or continuing noncompliance with Department of Health and Human Services (HHS) regulations at §45 CFR 46 or the requirements or determinations of the institutional review board (IRB); and suspension or termination of IRB approval.

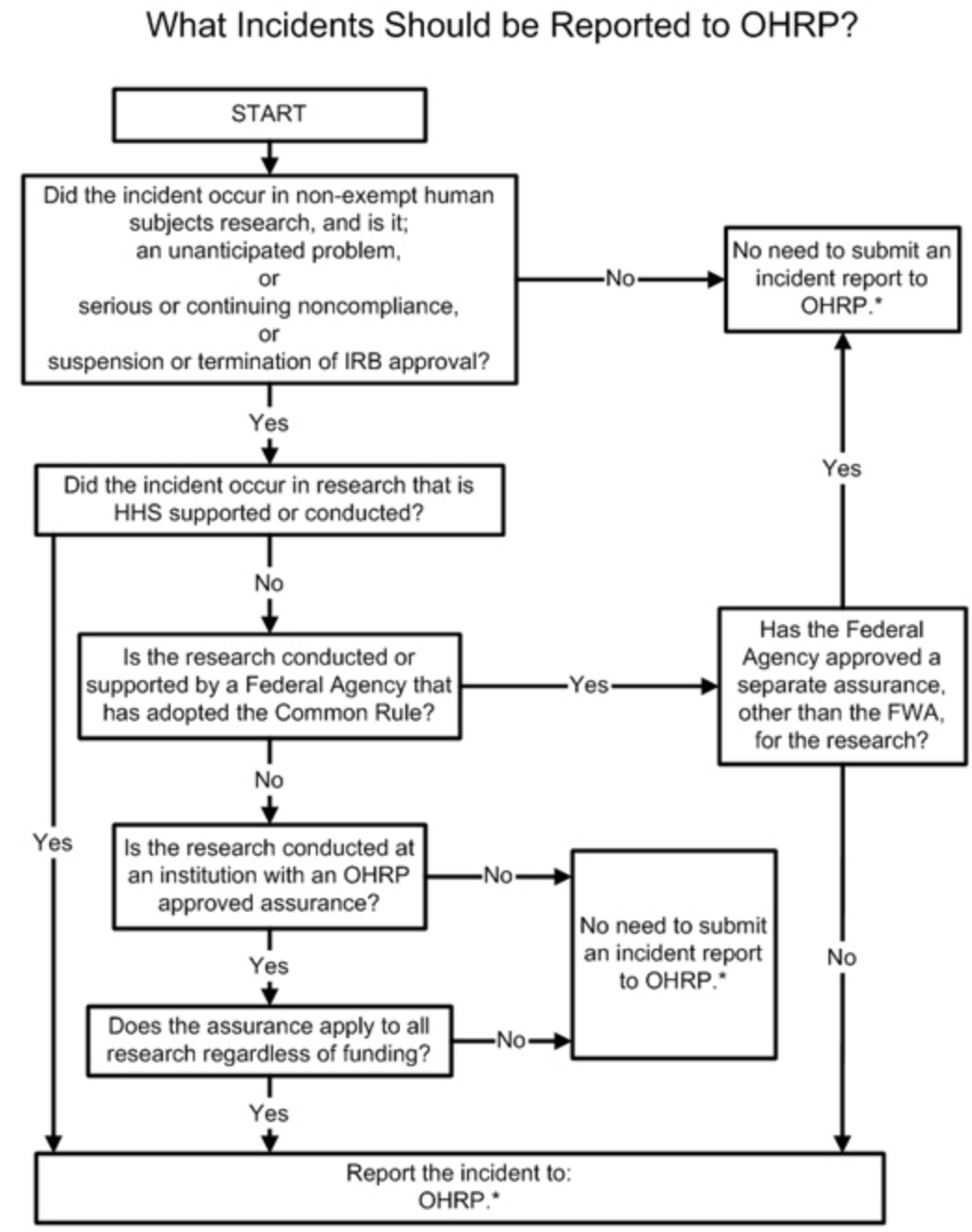
2. Guidance:

a. Applicability of Incident Reporting Requirements

In general, these reporting requirements apply to all nonexempt human subjects research that is: (a) conducted or supported by HHS; (b) conducted or supported by any non-HHS federal

department or agency that has adopted the Common Rule and is covered by a Federalwide Assurance (FWA) determined to be appropriate for such research; or (c) covered by an FWA, regardless of funding source.

Federal departments or agencies other than HHS that have adopted the Common Rule may determine that the FWA is not appropriate for certain research that they conduct or support. OHRP notes that these incident reporting requirements are **not** applicable to such research. In such cases, the institution should contact the non-HHS department or agency that supports the research about reporting requirements. See the decision chart below.



* Other reporting requirements may apply, whether or not a report to OHRP is required.

b. Information to be included in incident reports

To fulfill the regulatory requirements for reporting incidents, OHRP would consider it acceptable for an institution to comply with written procedures specifying that the following information be included in an incident report submitted to OHRP:

(1). For unanticipated problems involving risks to subjects or others:

- Name of the institution (e.g., university, hospital, foundation, school, etc.) conducting the research;
- Title of the research project and/or grant proposal in which the problem occurred;
- Name of the principal investigator on the protocol;
- Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);
- A detailed description of the problem; and
- Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.).

(2). For serious or continuing noncompliance:

- Name of the institution (e.g., university, hospital, foundation, school, etc.) conducting the research;
- Title of the research project and/or grant proposal in which the noncompliance occurred, or, for IRB or institutional noncompliance, the IRB or institution involved;
- Name of the principal investigator on the protocol, if applicable;
- Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);
- A detailed description of the noncompliance; and
- Actions the institution is taking or plans to take to address the noncompliance (e.g., educate the investigator, educate all research staff, educate the IRB or institutional official, develop or revise IRB written procedures, suspend the protocol, suspend the investigator, conduct random audits of the investigator or all investigators, etc.).

(3). For suspension or termination:

- Name of the institution (e.g., university, hospital, foundation, school, etc.) conducting the research;
- Title of the research project and/or grant proposal that was suspended or terminated;
- Name of the principal investigator on the protocol;
- Number of the research project assigned by the IRB that was suspended or terminated and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);

- A detailed description of the reason for the suspension or termination; and
- The actions the institution is taking or plans to take to address the suspension or termination (e.g., investigate alleged noncompliance, educate the investigator, educate all research staff, require monitoring of the investigator or the research project, etc.)

c. Time frame for reporting incidents

The regulations at 45 CFR 46.103(a) and (b) do not specify a time frame for reporting, except to say this must be done "promptly." For a more serious incident, this may mean reporting to OHRP within days. For a less serious incident, a few weeks may be sufficient. It may be appropriate to send an initial report, and indicate that a follow-up or final report will follow by the earlier of:

- a specific date; or
- when an investigation has been completed or a corrective action plan has been implemented.

3. OHRP focus on corrective actions when reviewing incident reports

When reviewing a report of an unanticipated problem, OHRP assesses most closely the adequacy of the actions taken by the institution to address the problem. Likewise, when reviewing reports of non-compliance or suspension or termination of IRB approval, OHRP assesses most closely the adequacy of the corrective actions taken by the institution. In particular, OHRP assesses whether or not the corrective actions will help ensure that the incident will not happen again, with the investigator or protocol in question, with any other investigator or protocol, or with the IRB. Therefore, OHRP recommends that, when appropriate, corrective actions be applied institution-wide.

XXXIII. Reporting Violations of the Georgia Institute of Technology Institutional Review Board Policies and Procedures

Reviewed: July 2024

Anyone with a concern about any aspect of research involving human subjects at Georgia Institute of Technology or who wants to report a violation of these Policies and Procedures may contact the Institutional Official, the IRB Chair, any IRB member, a Research Associate, or the IRB Director. Concerns may also be emailed to irb@gatech.edu. Reports made to the Office of Research Integrity Assurance will be delivered to the IRB Chair and the Institutional Official for further action.

No adverse action will be taken against anyone making a good-faith report. No Institute employee, committee member, student, or other person shall be discriminated against or be subject to any reprisal for reporting, in good faith, concerns or violations of regulations or standards under *Title 45 Code of Federal Regulations Part 46* or *Title 21 Code of Federal Regulations, Parts 50*, *56*, *312* or *812*. Persons with no formal relationship with the Georgia Institute of Technology are also encouraged to register their concerns, also without fear of reprisal or future discrimination.

XXXIV. Human Subjects Research Studies Approved Prior to the Implementation of the 2018 Common Rule

Reviewed: July 2024

The DHHS regulations pertaining to rights and welfare of subjects participating in research supported with federal funding specified in Title 45 Code of Federal Regulations Part 46, "Federal Policy for the Protection of Human Subjects" and including Subparts A, B, C, and D (referred to as the "Common Rule") were revised in 2018 (referred to as the "2018 Common Rule") and the revisions were implemented on January 21, 2019. All Georgia Tech human subjects research that was approved prior to January 21, 2019, remain regulated by the Common Rule regulations that were in effect when originally approved (referred to as "Pre-2018 Common Rule"). An explanation of the different regulations that apply to this subset of research is listed below.

A. Definition of Human Subjects, Identifiable Private Information, and Identifiable Biospecimen

The 2018 Common Rule re-defined the term "human subject" and added new terms regarding "identifiable private information" and "identifiable biospecimen," both of which were referred to in the new human subject definition. These terms provided more clarity in regards to what research is considered to be human subjects research and therefore, regulated under the Common Rule. However, for studies approved prior to the implementation of the 2018 Common Rule, the original definitions still apply.

B. Exempt Research

Under the Pre-2018 Common Rule, several exempt categories were limited in scope and differ greatly from the 2018 Common Rule exempt categories. The Pre-2018 Common Rule exempt categories are listed below and still apply to all Exempt research that was determined to be exempt prior to January 21, 2019.

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as
    (i) research on regular and special education instructional strategies, or

(ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research involving the use of educational tests (cognitive diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:

(i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and

(ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt, if:

(i) the human subjects are elected or appointed public officials or candidates for public office; or

(ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

5. Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:

(i) Public benefit or service programs;

(ii) procedures for obtaining benefits or services under those programs;

(iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

6. Taste and food quality evaluation and consumer acceptance studies,

(i) if wholesome foods without additives are consumed or

(ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

C. Continuing Review

The Pre-2018 Common Rule required all non-Exempt research (Expedited and Full Board studies) to be reviewed by the IRB and renewed at a minimum of once per year for as long as human subjects research activities continue. Therefore, all active non-Exempt research approved under the Pre-2018 Common Rule are required by the Georgia Tech IRB to submit continuing review applications so they may be reviewed and renewed at a minimum of once per year.

D. Consent Forms

The 2018 Common Rule added multiple sections and required information to the consent process and forms. However, as the Georgia Tech IRB does not require this information to be included in the consent process and forms for studies approved under the Pre-2018 Common Rule (e.g., Key Information, financially benefit from future medical discoveries, etc.).

E. Clinical Trials

The 2018 Common Rule defined the term “clinical trial” and added requirements for federally funded research that fit the description. The term clinical trial refers to a “research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes” (45 CFR 46.102). However, as this definition and the requirement to post the consent form within 60 after the last study visit did not exist in the Pre-2018 Common Rule, any study that fits this definition that was approved under the Pre-2018 Common Rule does not need to comply with this requirement.

Georgia Institute of Technology
Institutional Review Board
POLICIES & PROCEDURES

APPENDICES

Reviewed: July 2024

APPENDIX 1: Templates to be Utilized in Preparing Consent Documents for Collection of Data by Instructor/Researcher Enrolling Their Students

Template 1: Given to students at beginning of course

Template 2: To be signed before the end of the course. A third party will hold the consent documents until after grades are posted, and faculty will not know which students enroll until that time.

APPENDIX 2: Re-Analysis of Secondary Data from Human Subjects

APPENDIX 3: Certificates of Confidentiality

A. Food and Drug Administration (FDA) Certificates of Confidentiality
B. National Institute of Health (NIH) Funded Research and Certificates of Confidentiality

APPENDIX 4: Data Storage Guidelines

APPENDIX 5: Office for Human Research Protections (OHRP) Guidance on the Genetic Information Nondiscrimination Act:

A. GINA and the Criteria for IRB Approval of Research
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Appendix 1: Templates to be Utilized in Preparing Consent Documents for Collection of Data by Instructor/Researcher Enrolling Their Students

Template 1: Given to students at beginning of course

Georgia Institute of Technology
STUDY INFORMATION SHEET
Project Title:
Principal Investigator:
You are invited to participate in a research study. This study investigates _____. It will be in conjunction with your course _____ that I will teach this _____.

INFORMATION

The following activities are part of the normal curriculum of [name of course]. *[Describe activities, e.g. required writings, tests]*
At the end of the course, after grades have been submitted, I will ask for your written consent to review your class activities for the study described above. [*If audio-taping is involved, state:: I will also ask your consent to participate in an audio-taped interview regarding your experiences with this class.]* The interview will be no more than ____ hour(s) in length.

BENEFITS

The benefits are: _____.

RISKS

There are no foreseeable risks in participating in this study. No data will be analyzed until after grades are entered.

CONFIDENTIALITY

The following procedures will be followed to keep your personal information confidential in this study: We will comply with any applicable laws and regulations regarding confidentiality. To protect your privacy, your records will be kept under a code number rather than by name. Your records will be kept in locked files and only study staff will be allowed to look at them. Your name and any other fact that might point to you will not appear when results of this study are presented or published. The Georgia Institute of Technology IRB and the Office of Human Research Protections may look over study records during required reviews. *[If audio-taping is involved, add: "Access to the tapes of your interviews will be limited to research investigators and paid transcribers. Typed transcripts of these tapes will be made and in those typed transcripts pseudonyms will be used for all names of persons. At the conclusion of the study (xx-xx-xx), these tapes will be _____."]*
To make sure that this research is being carried out in the proper way, the Georgia Tech IRB will review study records.

CONTACT

If you have any questions about this study or its procedures, please contact _____.
If you feel you have not been treated according to the descriptions in this form, or that your rights as a participant have not been honored during the course of this project, you may contact the Office of Research Integrity Assurance at irb@gatech.edu.

PARTICIPATION

Your participation (allowing your class data to be used) in this study is voluntary. Refusal to participate will involve no penalty. If you decide to participate, you may withdraw from the study at any time without penalty. If you withdraw from the study your data will be returned to you or destroyed.

Template 2: To be signed before the end of the course. A third party will hold the consents until after grades are posted, and faculty will not know which students enroll until that time.

Georgia Institute of Technology
INFORMED CONSENT STATEMENT

Project Title:
Principal Investigator:

You are invited to participate in a research study. This study investigates _____. The purpose of this study is to _____.

INFORMATION

1. The following activities were part of the regular [name of course] curriculum of. [Describe activities, e.g. required writings, tests] If you volunteer for this study, the researchers will review your class activities as part of this study now that grades have been turned in.
2. Your participation in this study requires no additional time. {*If applicable, add the following: "…with the exception of an audio-taped interview regarding your experiences with _____ and lasting no more than _____ hour(s) in length."}*
3. In signing this consent statement, you agree to give permission for the researchers to use your materials {*and the audio-tapes*} for research purposes only. The transcribers will use pseudonyms to protect the identity of the participants. You may preview and make changes to the transcripts before they are analyzed.

BENEFITS

It is anticipated that you will benefit from your participation in the following ways: _____.

RISKS

There are no foreseeable risks or discomforts of any of the procedures to be used in this study.

CONFIDENTIALITY

The following procedures will be followed to keep your personal information confidential in this study: We will comply with any applicable laws and regulations regarding confidentiality. To protect your privacy, your records will be kept under a code number rather than by name. Your records will be kept in locked files and only study staff will be allowed to look at them. Your name and any other fact that might point to you will not appear when results of this study are presented or published. The Georgia Institute of Technology IRB and the Office of Human Research Protections may look over study records during required reviews. *]If audio-taping is involved, add: "Access to the tapes of your interviews will be limited to research investigators and paid transcribers. Typed transcripts of these tapes will be made and in those typed transcripts pseudonyms will be used for all names of persons. At the conclusion of the study (xx-xx-xx), these tapes will be _____."]*

To make sure that this research is being carried out in the proper way, the Georgia Tech IRB will review study records.

CONTACT

If you have any questions about this study or its procedures, you may contact the primary researcher, _____ at _____.

If you feel you have not been treated according to the descriptions in this form, or that your rights as a participant have not been honored during the course of this project, you may contact the Office of Research Integrity Assurance at irb@gatech.edu.

PARTICIPATION

Your participation in this study is voluntary; you may decline to participate without penalty. If you decide to participate, you may withdraw from the study at any time without penalty and without loss of benefits to which you are otherwise entitled. If you withdraw from the study before data collection is completed, your data will be returned to you or destroyed.

CONSENT

I have read this form and received a copy of it. I have had all my questions answered to my satisfaction. I agree to take part in this study.

Subject's signature_____Date_____

Person Obtaining Consent _____ _____

Name Printed Signature

Appendix 2: Re-Analysis of Secondary Data from Human Subjects

When previously collected data are being re-analyzed, the requirement for IRB approval may be waived, provided that:

a) the data will be analyzed in an anonymous manner,

and

b) the prior study was conducted under IRB approval;

or

c) research is re-analysis of publicly available datasets, provided the two conditions cited above apply;

or

d) research is being conducted entirely on census data.

Appendix 3: Certificates of Confidentiality

Certificates of Confidentiality (CoC) are issued by the National Institutes of Health (NIH) to protect identifiable research information from forced disclosure. The Food and Drug Administration handles requests for Certificate of Confidentiality protection for studies that obtain an Investigational New Drug (IND) authorization or other FDA authorization. A CoC allows the investigator and others who have access to research records to refuse to disclose identifying information on research participants in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level.

Certificates of Confidentiality may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation. By protecting researchers and institutions from being compelled to disclose information that would identify research subjects, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by assuring confidentiality and privacy to participants.

It should be noted that Certificates of Confidentiality have certain limitations. Typical language in a COC states, "[You]…are hereby authorized to protect the privacy of the individuals who are the subjects of the research *by withholding their names* and *other identifying characteristics*…."

Certificates of Confidentiality constitute an important tool to protect the privacy of research study participants, thus NIH encourages their appropriate use. Information is available on the NIH website. The Kiosk includes background information on Certificates, application instructions for extramural and intramural investigators, frequently asked questions, information on communicable disease reporting policy, and a list of contacts.

The Georgia Tech Institutional Review Board will require a Certificate of Confidentiality for studies that collect private personal information, the disclosure of which could put research subjects at risk. Since NIH will not issue a Certificate of Confidentiality unless the project has IRB approval, the Georgia Tech Office of Research Integrity Assurance will coordinate with the Principal Investigator to obtain the CoC. NIH will accept an IRB approval letter that is conditioned *only upon the issuance of a Certificate of Confidentiality*.

When a Certificate of Confidentiality will be obtained for a study, the enrolling human subjects must be informed during the consent process about the protections afforded by the certificate and any exceptions to that protection. Information should be included in the informed consent form, such as provided in these examples:

"We have obtained a Certificate of Confidentiality from the National Institutes of Health to help us keep your information confidential. This Certificate provides a way that researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal. A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information."

The following language should be included in the consent form if researchers intend to make voluntary disclosures about child abuse, intent to hurt self or others, or other disclosures:

"The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances."

[Identify circumstances that researchers intend to make voluntary disclosures.]

A. Food and Drug Administration (FDA) Certificates of Confidentiality

Projects involving Investigational New Drugs (INDs) or Investigational Device Exemptions (IDEs) should apply to the FDA when a Certificate of Confidentiality is appropriate. (Kevin Prohaska, D.O., M.P.H., Captain, U.S. Public Health Service Corps, The FDA has provided guidance on when a CoC is appropriate and provides instructions on how to request for a CoC. This guidance can be found at https://www.fda.gov/media/132966/download.

B. National Institute of Health (NIH) Funded Research and Certificates of Confidentiality

Under the NIH policy, as of October 1, 2017, NIH-funded researchers no longer have to request a CoC, nor do they receive an actual certificate. The CoC is issued automatically to NIH-funded grants, cooperative agreements, contracts and intramural research projects funded wholly or in part by the NIH that collects or uses identifiable, sensitive information. Compliance with the requirements of the law has become a term and condition of award. All research that was commenced or ongoing on or after December 13, 2016 and is within the scope of this policy is issued a Certificate through this policy.

Appendix 4: Data Storage Guidelines and Resources

The Office of Information Technology guidance on protecting and backing up sensitive data in electronic format.

Researchers should work with the technical lead in their college to prevent unauthorized or inadvertent release of human subjects' individually identifiable health information, protected health information (PHI), and any other sensitive information. In some cases, unauthorized or inadvertent releases can result in enforcement actions by federal agencies.

In the event of a data breach, investigators should immediately contact the Office of Information Technology AND the Office of Research Integrity Assurance for assistance and guidance, particularly when the disclosure of data poses a significant risk for the subjects. OIT's Information Security group will respond quickly to secure any breach in data security. The IRB will assist the investigator in determining when and whether it is necessary to inform subjects.

The Georgia Tech Library, offers assistance with data management plans. The Georgia Tech Library's website helps walks researchers step-by-step through the data management planning process. Sample NIH and NSF data management plans are available, as are links to guidelines for sharing and archiving data related to human subjects.

Scholarly Materials And Research @ Georgia Tech (SMARTech), also found on Georgia Tech's Library website, is an institutional repository available to researchers whose funding agency or other organizations do not maintain a data archive or repository that will accept research data. Researchers intending to use SMARTech should include the following information in their data management plans for submission to the IRB: *"Any dissertation and any sharable research data related to this project will be deposited into SMARTech, or Scholarly Materials And Research @ Georgia Tech. SMARTech is a trusted digital repository that captures the intellectual output of the Institute in support of its teaching and research missions. Digital materials in the repository are available to Georgia Tech and the world. All Georgia Tech dissertations are published via this mechanism, which is searchable through internet search engines such as Google. The Library and SMARTech are committed to adhering to the best practices of the profession applying to digital preservation."*
For more assistance with creating data management plans or using the SMARTech repository, contact the Research Data Librarian at the Georgia Tech Library.

Appendix 5: Office for Human Research Protections (OHRP) Guidance on the Genetic Information Nondiscrimination Act

This guidance represents OHRP's current thinking on this topic and should be viewed as recommendations unless specific regulatory requirements are cited. The use of the word must in OHRP guidance means that something is required under HHS regulations at §45CFR46. The use of the word should in OHRP guidance means that something is recommended or suggested, but not required. An institution may use an alternative approach if the approach satisfies the requirements of the HHS regulations at §45CFR46. OHRP is available to discuss alternative approaches at 240-453-6900 or 866-447-4777.

Date: March 24, 2009

Scope: This document applies to non-exempt human subjects research conducted or supported by HHS. It provides background information regarding the Genetic Information Nondiscrimination Act of 2008 (GINA) and discusses some of the implications of GINA for investigators who conduct, and institutional review boards (IRBs) that review, non-exempt human subjects research involving genetic testing or the collection of genetic information (hereinafter referred to as "genetic research"), particularly with respect to the criteria for IRB approval of research and the requirements for obtaining informed consent.

The information presented in the background section of this document is intended for general information purposes only. While the background section does not cover all of the specifics of GINA, it does provide an explanation of the statute to assist those involved in the conduct or oversight of research to understand the law and its prohibitions related to discrimination based on genetic information in (a) coverage provided either by health insurers or by employment-based group health plans (hereinafter referred to as "health coverage"), and (b) employment. This information should not be considered legal advice. In addition, some of the provisions of GINA discussed involve issues for which the rules have not been finalized, and this information is subject to revision based on publication of regulations.

Target Audience: Investigators who conduct, and IRBs that review, genetic research involving human subjects that is conducted or supported by HHS.

Background on GINA:
GINA is a Federal law that prohibits discrimination in health coverage and employment based on genetic information. GINA, together with already existing nondiscrimination provisions of the Health Insurance Portability and Accountability Act, generally prohibits health insurers or health plan administrators from requesting or requiring genetic information of an

individual or an individual's family members, or using such information for decisions regarding coverage, rates, or preexisting conditions. GINA also prohibits employers from using genetic information for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment. The parts of the law relating to health coverage (Title I) generally will take effect between May 22, 2009, and May 21, 2010, and those relating to employment (Title II) will take effect on November 21, 2009.(1) GINA requires regulations pertaining to both titles to be completed by May 2009. Once GINA takes effect, it generally will prohibit discrimination based on genetic information in connection with health coverage and employment, no matter when the information was collected.

GINA provides a baseline level of protection against genetic discrimination for all Americans. Many states already have laws that protect against genetic discrimination in health insurance and employment situations. However, the degree of protection they provide varies widely, and while most provisions are less protective than GINA, some are more protective. All entities that are subject to GINA must, at a minimum, comply with all applicable GINA requirements, and may also need to comply with more protective State laws.

GINA defines *genetic information* as information about:

- An individual's genetic tests (including genetic tests done as part of a research study);
- Genetic tests of an individual's family members (defined as dependents and up to and including 4th degree relatives);
- Genetic tests of any fetus of an individual or family member who is a pregnant woman, and genetic tests of any embryo legally held by an individual or family member utilizing assisted reproductive technology;
- The manifestation of a disease or disorder in an individual's family members (family history); or
- Any request for, or receipt of, genetic services or participation in clinical research that includes genetic services (genetic testing, counseling, or education) by an individual or an individual's family members.

Genetic information does not include information about the sex or age of any individual.
GINA defines a genetic test as an analysis of human DNA, RNA, chromosomes, proteins, or metabolites that detect genotypes, mutations, or chromosomal changes. Routine tests that do not detect genotypes, mutations, or chromosomal changes, such as complete blood counts, cholesterol tests, and liver enzyme tests, are not considered genetic tests under GINA. Also, under GINA, genetic tests do not include analyses of proteins or metabolites that are directly related to a manifested disease, disorder, or pathological condition that

could reasonably be detected by a health care professional with appropriate training and expertise in the field of medicine involved.

GINA includes a "research exception" to the general prohibition against health insurers or group health plans requesting that an individual undergo a genetic test. This exception allows health insurers and group health plans engaged in research to request (but not require) that an individual undergo a genetic test. This exception permits the request to be made but imposes the following requirements:

- The request must be made pursuant to research that complies with HHS regulations at §45CFR46, or equivalent Federal regulations, and any applicable state or local laws for the protection of human subjects in research;
- There must be clear indication that participation is voluntary and that non-compliance has no effect on enrollment or premiums or contribution amounts;
- No genetic information collected or acquired as part of the research may be used for underwriting purposes;
- The health insurer or group health plan must notify the Federal government in writing that it is conducting activities pursuant to this research exception and provide a description of the activities conducted; and
- The health insurer or group health plan must comply with any future conditions that the Federal government may require for activities conducted under this research exception.

GINA's provisions prohibiting discrimination in health coverage based on genetic information do not extend to life insurance, disability insurance, or long-term care insurance. For example, GINA does not make it illegal for a life insurance company to discriminate based on genetic information. In addition, GINA's provisions prohibiting discrimination by employers based on genetic information generally do not apply to employers with fewer than 15 employees. For health coverage provided by a health insurer to individuals, GINA does not prohibit the health insurer from determining eligibility or premium rates for an individual based on the manifestation of a disease or disorder in that individual. For employment-based health coverage provided by group health plans, GINA permits the overall premium rate for an employer to be increased because of the manifestation of a disease or disorder of an individual enrolled in the plan, but the manifested disease or disorder of one individual cannot be used as genetic information about other group members to further increase the premium. GINA also does not prohibit health insurers or health plan administrators from obtaining and using genetic test results in making payment determinations.

For additional details regarding the provisions of GINA see http://www.genome.gov/Pages/PolicyEthics/GeneticDiscrimination/GINAInfoDoc.pdf.

Guidance:

Given that GINA has implications regarding the actual or perceived risks of genetic research and an individual's willingness to participate in such research, investigators and IRBs should be aware of the protections provided by GINA as well as the limitations in the law's scope and effect. IRBs should consider the provisions of GINA when assessing whether genetic research satisfies the criteria required for IRB approval of research, particularly whether the risks are minimized and reasonable in relation to anticipated benefits and whether there are adequate provisions in place to protect the privacy of subjects and maintain the confidentiality of their data. GINA is also relevant to informed consent. When investigators develop, and IRBs review, consent processes and documents for genetic research, they should consider whether and how the protections provided by GINA should be reflected in the consent document's description of risks and provisions for assuring the confidentiality of the data.

A. GINA and the Criteria for IRB Approval of Research

When reviewing proposed or ongoing genetic research, IRBs should consider the protections provided by GINA when determining whether the research satisfies the following criteria required for IRB approval of research:

- Risks to subjects are minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk; and (ii) whenever appropriate, by using procedures which are already being performed on the subjects for diagnostic or treatment purposes (§45CFR46.111(a)(1));
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result (§45CFR46.111(a)(2)); and
- When appropriate, there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of data (§45CFR46.111(a)(7)).

Among the risks typically associated with genetic research, investigators, IRBs, and research subject advocates, among others, have identified the potential adverse impact on insurability or employability if genetic information about the subject obtained as part of the research was disclosed to, or sought by, insurers or employers. When the provisions of GINA take effect, the risk of such harms will be decreased with respect to health coverage and most employment. Since a decrease in risk should favorably affect the risk-benefit assessment for genetic research, the protections provided by GINA have direct

relevance for IRBs that are assessing whether genetic research satisfies the criteria under §45CFR46.111(a)(1), (2), and (7).

Even though the provisions of GINA related to health coverage generally will take effect between May 22, 2009, and May 21, 2010, and those related to employment will take effect on November 21, 2009, investigators and IRBs should be aware that the protections provided by GINA are pertinent to genetic research that is conducted prior to these effective dates because these protections eventually will extend to genetic information obtained as part of any research study regardless of when the research was conducted. Therefore, IRBs conducting initial or continuing review of genetic research prior to GINA's stipulated effective dates should take into account the protections to be provided by GINA when assessing whether such research satisfies the criteria required for IRB approval of research referenced above.

When making the above determinations required under §45CFR46.111(a), IRBs also need to be cognizant that (1) GINA's provisions prohibiting discrimination in health coverage based on genetic information do not extend to life insurance, disability insurance, or long-term care insurance; and (2) GINA's provisions prohibiting discrimination by employers based on genetic information generally do not apply to employers with fewer than 15 employees.

B. GINA and the Requirements for Informed Consent

When investigators develop, and IRBs review, consent processes and documents for genetic research, they should consider the protections provided by GINA, particularly with respect to the following elements of informed consent that must be provided to subjects (unless an IRB has approved an alteration or waiver of these requirements in accordance with the requirements of HHS regulations at §45CFR46.116(e) or (f)):

- A description of any reasonably foreseeable risks or discomforts to the subjects (§45CFR46.116(b)(2)); and
- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained (§45CFR46.116(b)(5)).

Investigators and IRBs must ensure that descriptions of the reasonably foreseeable risks of genetic research and any statements describing the extent to which confidentiality of records identifying the subject will be maintained do not overstate the protections provided by GINA (§45CFR46.116). Key points for investigators and IRBs to consider when describing these protections include the following:

- The provisions of GINA related to health coverage generally will take effect between May 22, 2009, and May 21, 2010, and those related to employment will take effect on November 21, 2009.

- The discrimination protections provided by GINA address health coverage and employment only.
- GINA's provisions prohibiting discrimination in health coverage based on genetic information do not extend to life insurance, disability insurance, or long-term care insurance. Therefore, to the extent that the risks of genetic research include potential adverse impact on a subject's ability to obtain life insurance, disability insurance, or long-term care insurance if genetic information about the subject obtained as part of the research was disclosed to or sought by such insurers, GINA has no effect on these risks.
- GINA generally does not apply to employers with fewer than 15 employees. Therefore, subjects who are or will be employed by such employers receive none of the GINA protections that prohibit discrimination in employment on the basis of genetic information.
-

Even though, as explained above, the provisions of GINA related to health coverage do not take effect until sometime within a year of May 21, 2009, and those related to employment do not take effect until November 21, 2009, investigators and IRBs need to be aware that GINA has implications for how risks are described for genetic research conducted prior to these effective dates.

Regardless of when genetic information was obtained or collected, GINA restricts the use of such information as soon as GINA becomes effective for a particular plan or insurance policy. For example, even if an individual participated in a research study involving genetic testing in January 2009, a health insurer or health plan administrator, once GINA's protections related to health coverage take effect, will be prohibited from (1) requesting information about the results of the genetic tests performed in that research study or about the individual's participation in that research study (unless the health insurer or health plan administrator has satisfied the requirements of the research exception discussed in the background section above), and (2) using such information for decisions regarding coverage, rates, or preexisting conditions for that individual if such information is disclosed in some way to the insurer or health plan administrator.

Likewise, effective November 21, 2009, GINA generally will prohibit employers with 15 or more employees from using genetic information for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment, *regardless of when the information was obtained or collected*. For example, even if an individual participated in a research study involving genetic counseling in January 2009, an employer with 15 or more employees, as of November 21, 2009, will be prohibited from using genetic information resulting from that individual's participation in that research for hiring, firing, or promotion decisions or for any decisions regarding terms of employment for that individual.

OHRP recommends that for genetic research undergoing initial or continuing review investigators and IRBs consider whether consent processes and documents should include language regarding the protections provided by GINA, and if so, ensure that such language accurately describes the impact of GINA on the risks and confidentiality protections for such research. The following is one example of sample language regarding the protections provided under GINA that investigators and IRBs could consider including in informed consent documents for such research, if it is determined that including such language is appropriate:

> *A new Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:*
>
> > *Health insurance companies and group health plans may not request your genetic information that we get from this research. (2)*
> >
> > *Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.*
> >
> > *Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.*
>
> *All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009.*
>
> *Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. (3)*

IRBs should feel free to revise the sample language above as appropriate based on the nature of the research and the types of human subjects involved.

If you have specific questions about how to apply this guidance, please contact OHRP by phone at (866) 447-4777 (toll-free within the U.S.) or (240) 453-6900, or by e-mail at ohrp@hhs.gov.

Footnotes:

1. The effective date of the insurance provisions is not the same in all cases because for group health plans, Title I will take effect at the start of the group health plan's first year beginning after May 21, 2009. Because some health plans do not designate their "plan years" to correspond to a calendar year, there will be variation among plans as to when Title I takes effect for the plans. However, for individual health insurers, GINA will take effect May 22, 2009.
2. Note that if an insurance company or health plan administrator is engaged in the research in accordance with the requirements of the research exception, this bullet should be modified accordingly.
3. For genetic research that involves determining whether subjects have an already manifest genetic disease or disorder, investigators and IRBs may wish to consider including additional language in the informed consent document indicating that GINA does not prohibit discrimination on the basis of an already manifest genetic disease or disorder.

Appendix 6: Template Addenda for Consent and Additional Information for Subjects Whose Biological Specimens Are Utilized

Refer to "Research Involving the Collection of Human Biologic Specimens" in these *Policies & Procedures* for a complete discussion of protection considerations for subjects whose biological specimens are being utilized in research. In these Appendices, the IRB presents consent form addendum templates and additional information for use with subjects whose specimens will be identified (coded) and for those whose specimens will not be identified (not coded).

A. Consent Addendum for Storing Blood, Tissue or Body Fluid <u>with Identifying Information</u>

Addendum to Consent for Participation in:

(*Identify here by IRB number, title and name of the Principal Investigator the protocol to which this will be added)*

You are asked to give permission for some of your blood, tissue or body fluid (collectively referred to as "specimens") which will be collected in this research study to be stored for future medical research studies.

The specimens will be stored at the Georgia Institute of Technology, or another site. Your name and other personal information will be removed from the specimens and replaced with a code. All identifying information including your name and medical record number will be removed from the specimens and replaced with a code. Dr. _____ and his/her associates will have access to the specimens and the code which links the specimen to you. There is no cost to you or your insurance company for the storage and use of the specimens.

Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of those records, including personal information about you. When disclosure is required, the Georgia Institute of Technology will take all reasonable steps to protect the privacy of your personal information.

By signing this form, you will donate the specimens for medical research purposes. Your donation does not entitle you to compensation from any commercial use of the products that may be derived from the specimen. The research studies in which the specimens may be used have not yet been determined, but they may involve genetic research. Before any research involving the specimens is conducted, the Georgia Institute of Technology Institutional Review Board (IRB) will review and approve the research proposal.

In some cases, the IRB may require that you be contacted and asked for your consent to participate in the specific research study in which the specimens will be used. You have the right not to participate in any research study for which your consent is sought. Refusal to participate will not jeopardize your medical care or result in loss of benefits to which you are entitled.

In other cases, the IRB may require that you be notified about the results of a research study in which the specimens were used. You have the right to be told the results and their meaning, or to decide not to be told of those results, or to have the information sent directly to your personal physician.

You are asked to provide your permanent contact information and agree that it may be used by Dr. _____ and his/her associates if it necessary to contact you to ask your consent to participate in a specific research study or to notify you about the results of the study.

The specimens may be shared with other institutions, and research studies may be conducted at several locations at the same time. Non-identifying personal information about you will be provided to investigators from other institutions.

If in the future you should decide that you no longer wish for the specimens to be stored, you may contact Dr. _____and/or his/her associates at the Georgia Institute of Technology at (404)___ _____ or the Institutional Review Board at (404) 894-6949 and request that the specimens be disposed of according to standard medical research procedures. If you do not make such a request, the specimens will be stored indefinitely. They may be disposed of at any time at the discretion of the investigators.

Before signing this consent form, please read the brochure entitled ***Information About Storage and Use of Specimens With Identifying Information*** that is designed to answer your questions. It will be provided to you by the researcher.

Please check which course of action is to be followed in case the investigators cannot find you after reasonable time and effort, even though you provide your permanent contact information:

_____I agree to allow the specimens to continue to be stored with identifying information, for as-yet-undesignated purposes that may include genetic research.

_____I request that the identifying code be removed from the specimens; after that is done, the specimens may continue to be stored and used for as-yet-undesignated purposes that may include genetic research.

_____I request that the identifying code be removed from the specimens; after that is done the specimens may continue to be stored and used for as-yet-undesignated purposes NOT INCLUDING genetic research.

_____I request that the specimens be disposed of.

I consent to the donation and storage of the specimens, as described above.

_____ _____

Name of Subject Date

B. Informational Brochure with Information about Storage and Use of Specimens with Identifying Information

This brochure provides information that may help you decide whether to allow some of your blood, tissue and/or body fluid (specimens) which will be collected as part of this research study to be stored and used for future medical research.

WHAT WILL HAPPEN TO THE SPECIMEN?

The specimens will be processed for storage, catalogued and placed in a secured facility at the Georgia Institute of Technology, or another site. All identifying information, including your name and medical record number, will be removed from the specimens. The specimens will be given a unique identifier (code).

The researcher in this study and his/her associates will have access to the specimens and the code which links the specimens to you.

WILL RESEARCH RECORDS AND PERSONAL INFORMATION BE KEPT PRIVATE?

Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of those records, including personal information about you. When disclosure is required, the Georgia Institute of Technology will take all reasonable measures to protect the privacy of your personal information.

WILL I BE COMPENSATED FOR MY DONATION?

You will be informed during the consent process regarding compensation, if any. U.S. Tax Law requires that a 1099-misc be issued if U.S. tax residents receive $600 or more per calendar year. If non-U.S. tax residents receive more than $75, mandatory 30% withholding is required. Your address and Tax I.D. may be collected for compensation purposes only. This information will be shared only with the Georgia Tech department that issues compensation, if any, for your participation. This information will be shared only with the Georgia Tech department that issues compensation, if any, for your participation.

IS THERE ANY COST FOR STORAGE OF THE SPECIMENS?

There is no cost to you or your insurance company for the storage and use of the specimens.

WHO OWNS THE SPECIMENS?

By signing the consent form, you will donate the specimens for medical research purposes. Your donation does not entitle you to compensation from any commercial use of the products that may be derived from the specimens.

HOW WILL THE SPECIMENS BE USED IN THE FUTURE?

The research studies in which the specimens may be used have not yet been determined. The studies may involve genetic research. Genetic research is about finding the specific location of genes, learning how genes work, and developing treatments and cures for diseases which are genetically based.

Before any research involving the specimens is conducted, the Georgia Tech IRB will review and approve the research proposal. Board members include scientists, non-scientists, and community representatives. The purpose of the IRB is to assure that the interests of individuals participating in research studies are well protected.

WILL RESEARCHERS SEEK CONSENT TO DO FUTURE STUDIES INVOLVING THE SPECIMENS?

In some cases, the IRB may require that you be contacted and asked for your consent to participate in the specific research study in which the specimens will be used. You have the right not to participate in any research study for which your consent is sought. Refusal to participate will not jeopardize your medical care or result in loss of benefits to which you are entitled.

WILL YOU RECEIVE STUDY RESULTS OF RESEARCH INVOLVING YOUR SPECIMENS?

There may be times when the IRB will require that you be notified about the results of a research study in which your specimens were used. You have the right to be told of the results and their meaning, or to decide not to be told of those results, or to have the information sent directly to your personal physician.

HOW WILL RESEARCHERS FIND YOU IN THE FUTURE?

If you decide to allow the specimens to be stored and used in future medical research studies, you will be asked to provide your permanent contact information. Your permanent contact information will be used

by the researchers and their associates in this study when it is necessary to contact you to seek your consent to participate in a specific research study or to notify you about the results of that study.

If you allow your specimens to be stored with identifying information, you will be asked to choose, at the time you sign the consent form, a course of action that will be taken in the event that the researchers are unable to locate you in the future, even with your permanent contact information. The options include allowing continued storage and use of your specimens with the identifying code remaining, continued storage and use of the specimens after removing the identifying code, and disposing of the specimens according to standard medical procedures.

WILL THE SPECIMENS BE SHARED WITH OTHER INSTITUTIONS?

The specimens may be shared with researchers from other institutions. Research studies may be conducted at several locations at the same time.

No identifying personal information about you will be provided to researchers from other institutions that will use the specimens.

HOW LONG WILL THE SPECIMENS BE STORED?

The specimens will be stored indefinitely. Specimens may also be disposed of at any time at the discretion of the investigators, using standard medical procedures. If in the future you should decide that you no longer wish for the specimens to be stored, you may contact the researcher and/or his/her associates on the study in which you are participating. You may also contact the Georgia Tech IRB and request that the specimens be disposed of.

C. Consent Addendum for Storing Blood, Tissue or Body Fluid without Identifying Information

Addendum to Consent for Participation in:

(*Identify here by IRB number, title and name of the Principal Investigator the protocol to which this will be added)*

You are asked to give permission for some of your blood, tissue or body fluid (collectively referred to as "specimens") which will be collected in this research study to be stored for future medical research studies.

The specimens will be stored at the Georgia Institute of Technology or another site. All identifying information including your name and medical record number will be removed from the specimens and will not be retained. As a result, it will be impossible to connect you with the specimens. This means that you will be unable to learn about the studies in which the specimen was used and any findings of those studies which relate to the specimens. There is no cost to you or your insurance company for the storage and use of the specimens.

By signing this form, you will donate the specimens for medical research purposes. Your donation does not entitle you to compensation from any commercial use of the products that may be derived from the specimens. The research studies in which the specimens may be used have not yet been determined. The specimens may be shared with other institutions and research studies may be conducted at several locations at the same time.

The specimens will be stored indefinitely.

Before signing this consent form, please read the brochure entitled ***Information About Storage and Use of Specimens Without Identifying Information*** that is designed to answer your questions.
Check one below:

___ I consent to the donation and storage of the specimens, as described above, for as-yet-undesignated purposes that may include genetic research.

___ I consent to donation and storage of the specimens as described above, for as-yet-undesignated purposes **NOT INCLUDING** genetic research.

_____ _____
Name of Subject Date

D. Information about Storage and Use of Specimens without Identifying Information

The following information may help you decide whether to allow some of your blood, tissue and/or body fluid (specimens) which will be collected as part of this research study to be stored and used for future medical research.

WHAT WILL HAPPEN TO THE SPECIMEN?

The specimen will be processed for storage, catalogued and placed in a secured facility at the Georgia Institute of Technology or another site. All identifying information, including your name and medical record number, will be removed from the specimen and will not be retained. As a result, it will be impossible to connect you with the specimen. Some basic information such as your age, gender and diagnosis may be retained with the specimen.

IS THERE ANY COST FOR STORAGE OF THE SPECIMEN?

There is no cost to you or your insurance company for the storage and use of the specimen.

WHO OWNS THE SPECIMEN?

By signing the consent form, you will have donated the specimen for medical research purposes. Your donation does not entitle you to compensation from any commercial use of the products that may be derived from the specimen.

WILL I BE COMPENSATED FOR MY DONATION?

You will be informed during the consent process regarding compensation, if any. U.S. Tax Law requires that a 1099-misc be issued if U.S. tax residents receive $600 or more per calendar year. If non-U.S. tax residents receive more than $75, mandatory 30% withholding is required. Your address and Tax I.D. may be collected for compensation purposes only. This information will be shared only with the Georgia Tech department that issues compensation, if any, for your participation. This information will be shared only with the Georgia Tech department that issues compensation, if any, for your participation.

HOW WILL THE SPECIMEN BE USED IN THE FUTURE?

The research studies in which the specimen may be used have not yet been determined. Some studies may involve genetic research. Genetic research is about finding the specific location of genes on chromosomes,

learning how genes work, and developing treatments and cures for diseases which are genetically based. If you sign the consent form, you may choose whether or not to allow the specimen to be used in genetic research.

Because it will be impossible to connect you with the specimen, you will not be contacted in the future about any planned studies involving the specimen. However, all such studies must be reviewed and approved by the Georgia Institute of Technology Institutional Review Board. The IRB members include scientists, non-scientists, and community representatives. The purpose of the IRB is to assure that the interests of individuals participating in research studies are well protected.

The specimen may be shared with researchers from other institutions. Research studies may be conducted at several locations at the same time.

WILL I RECEIVE STUDY RESULTS OF RESEARCH INVOLVING THE SPECIMEN?

Because it is impossible to connect you with the specimen, you will be unable to learn about the studies in which the specimen was used and any findings from those studies which relate to the specimen. This is true for all research on the specimen, including any genetic research.

HOW LONG WILL THE SPECIMEN BE STORED?

The specimen will be stored indefinitely.

Appendix 7: Sample Short Form Written Consent Document for Subjects Who Do Not Speak English

This document must be written in a language understandable to the subject

Consent to Participate in Research

You are being asked to participate in a research study. The investigator is _____Professor of XX_____ at the Georgia Institute of Technology in Atlanta, Georgia USA.

Before you agree, the investigator must tell you about (i) the purposes, procedures, and duration of the research; (ii) any procedures which are experimental; (iii) any reasonably foreseeable risks, discomforts, and benefits of the research; (iv) any potentially beneficial alternative procedures or treatments; and (v) how confidentiality will be maintained.

Where applicable, the investigator must also tell you about (i) any available compensation or medical treatment if injury occurs; (ii) the possibility of unforeseeable risks; (iii) circumstances when the investigator may halt your participation; (iv) any added costs to you; (v) what happens if you decide to stop participating; (vi) when you will be told about new findings which may affect your willingness to participate; and (vii) how many people will be in the study.

U.S. Tax Law requires a mandatory withholding of 30% for nonresident alien payments of any type. Therefore, your address and citizenship/visa status may be collected for compensation purposes only. This information will be shared only with the Georgia Tech department that issues compensation, if any, for your participation.

If you agree to participate, you must be given a signed copy of this document and a written summary of the research.

You may contact ____Principal Investigator____ at ___phone number__ any time you have questions about the research.

You may contact the Georgia Institute of Technology's Office of Research Integrity Assurance at irb@gatech.edu if you have questions about your rights as a research subject or what to do if you are injured.

Your participation in this research is voluntary, and you will not be penalized or lose benefits if you refuse to participate or decide to stop.

Signing this document means that the research study, including the above information, has been described to you orally, and that you voluntarily agree to participate.

_____ Date

Signature of Participant

_____ Date

Signature of Witness

Appendix 8: Comparison of FDA and HHS Human Subject Protection Regulations

FDA Regulations	HHS Regulations
56.101 Scope IRBs that review clinical investigations regulated by the FDA under sections 505(i), 507(d), and 520(g) of the act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the FDA, including food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products.	46.101 Scope All research involving human subjects conducted or supported by HHS or conducted in an institution that agrees to assume responsibility for the research in accordance with §45CFR46 regardless of the source of funding.
56.102 and 50.3 Definitions Definitions for *"Act"; "Application for research or marketing permit"; "Emergency use"; "Sponsor"; "Sponsor-investigator"; "Test article"* do not have comparable terms defined in §45CFR46. FDA has defined *"clinical investigation"* to be synonymous with *"research". "Clinical investigation"* means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA...or the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. *"Human subject"* means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient. *"Institutional Review Board"* means any board, committee, or other group formally designated by an institution to review, to approve the initiation or, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The term has the same meaning as the phrase *"institutional review committee"* as used in section 520(g) of the act.	46.102 Definitions Definitions for *"Department or agency head"; "Certification"* do not have comparable terms defined in §21CFR50 or 56 HHS has defined *"research"* as a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. The definition also includes research development, testing and evaluation, and research undertaken by students for the purpose of independent study, theses or dissertations. HHS has defined *"Research subject to regulation"* and similar terms as intending to encompass those research activities for which a federal department or agency has specific responsibility for regulating as a research activity, (for example, Investigational New Drug requirements administered by the FDA). *"Human subject"* means a living individual about whom an investigator conducting research obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. Included in the definition of human subject are human embryos, fetuses, and any human tissue or fluids. *"IRB"* means an institutional review board established in accord with and for the purposes expressed in this policy.
Definitions for "IRB approval"; "Minimal Risk; "Institution"; Legally authorized representative" are identical.	

FDA Regulations	HHS Regulations
56.103 Circumstances in which IRB review is required. Except as provided in 56.104 and 56.105, any clinical investigation which must meet the requirements for prior submission to the FDA or considered in support of an application for a research or marketing permit must have been reviewed and approved by, and remained subject to continuing review by, an IRB meeting the requirements of this part. [In diverging from the assurance requirement, FDA stated its belief that it is inappropriate for it to adopt the assurance mechanism. The benefits of assurance from IRBs that are subject to FDA jurisdiction, but not otherwise to HHS jurisdiction, do not justify the increased administrative burdens that would result from an assurance system. FDA relies on its Bioresearch Monitoring Program, along with its educational efforts, to assure compliance with these regulations.]	46.103 Assuring compliance with this policy--research conducted or supported by any Federal Department or Agency Sections dealing with assurances and certifications are unique to the common rule and the HHS regulations.
56.104 Exemptions from IRB requirement a. Any investigation which commenced before 7/27/81, and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before 7/27/81. b. Any investigation that commenced before 7/27/81 and was not otherwise subject to requirements for IRB review under FDA regulations before that date c. Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review.	46.104(d) Exemptions from this policy (1) Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods. (2) Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met: (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects; (ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

FDA Regulations	HHS Regulations
	(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7). (3)(i) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met: (A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects; (B) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or (C) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7). (ii) For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else. (iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

FDA Regulations	HHS Regulations
	(4) Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met: (i) The identifiable private information or identifiable biospecimens are publicly available; (ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects; (iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of “health care operations” or “research” as those terms are defined at 45 CFR 164.501 or for “public health activities and purposes” as described under 45 CFR 164.512(b); or (iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 *et seq.* (5) Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures,

FDA Regulations	HHS Regulations
	or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended. (i) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.
Identical Exemption: *Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe....*	
56.105 Waiver of IRB requirement. On the application of a sponsor or sponsor-investigator, the FDA may waive any of the requirements contained in these regulations, including the requirement for IRB review, for specific research activities or for classes of research activities, otherwise covered by these regulations.	No comparable provision.
56.107 and 46.107 IRB Membership requirements are identical	
56.108 and 46.108 "IRB functions and operations" are virtually identical except 56.108 requires reporting to the FDA; 46.108 requires reporting to the department or agency head.	
56.109 and 46.109 "IRB review of research" are virtually identical with the following exceptions: • 46.109(c) refers to the criteria in .117 for waiving the requirement for a signed consent form -- .117 is not included in FDA's regulations because FDA does not regulate research in which "the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality." • 56.109(c) and (e) contain additional language related to FDA's emergency research rule; HHS published identical criteria for emergency research in a Secretarial announcement of waiver of the applicability of §45CFR46, 10/2/96.	
56.110 and 46.110 "Expedited Review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research" are virtually identical, except: • 56.110 refers to the FDA and 46.110 refers to the Secretary, HHS, or the department or agency head	

FDA Regulations	HHS Regulations
• 56.110(d) states "The FDA may restrict, suspend, or terminate an institution's or IRB's use of the expedited review procedure **when necessary to protect the rights or welfare of subjects**." 46.110(d)states that "The department or agency head may restrict, suspend, terminate, **or choose not to authorize** an institution's or IRB's use of the expedited review procedures."	
56.111 and 46.111 "Criteria for IRB approval of Research" are virtually identical except 56.111 contains references to sections in part 50 and 46.111 contains references to sections in part 46. Furthermore, 46.111 contains information about Limited IRB Review and Broad consent, which is not in 56.111.	
56.112 and 46.112 "Review by institution" are identical.	
56.113 and 46.113 "Suspension or termination of IRB approval of research" are virtually identical except 56.113 refers to FDA and 46.113 refers to the department or agency head.	
56.114 Cooperative research In complying with these regulations, institutions involved in **multi-institutional studies** may use joint review, reliance upon the review of another qualified IRB, or similar arrangements aimed at avoidance of duplication of effort.	46.114 Cooperative research Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. With the approval of the department or agency head, an institution participating in a **cooperative project** may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.
56.115 and 46.115 "IRB Records" are virtually identical except • The list of IRB members required by 56.115(a)(5) is cross-referenced in 46.115(a)(5) to 46.103(b)(3) • 56.115(b) refers to FDA rather than the department or agency • 56.115(c) states that "The FDA may refuse to consider a clinical investigation...if the institution or the IRB that reviewed the investigation refuses to allow an inspection under this section." Part 46does not contain a comparable requirement.	
56.120 Lesser administrative actions The agency may 1. Withhold approval of new studies; 2. Direct that no new subjects be added to ongoing studies; 3. Terminate ongoing studies when doing so would not endanger the subjects; or 4. When the apparent non-compliance creates a significant threat to the rights and welfare of human subjects, notify relevant State and Federal regulatory agencies and other parties with a direct interest in the agency's action of the deficiencies in the operation of the IRB. The parent institution is presumed to be responsible for the operation of an IRB, and FDA will ordinarily direct any administrative action against the institution. However,	46.123 Early termination of research support; Evaluation of applications and proposals. 1. The department or agency head may require that...support for any project be terminated or suspended...when the department or agency head finds an institution has materially failed to comply with the terms of this policy. 2. In making decisions about supporting or approving applications or proposals...the department or agency head may take into account...factors such as whether the applicant has been subject to a termination or suspension under...this section and whether the applicant or the person or persons who would direct or has directed the scientific and technical aspects of an activity has, in the judgment of the department...materially failed to discharge responsibility for the protection of the rights and welfare of human subjects

FDA Regulations	HHS Regulations
depending on the evidence of responsibility for deficiencies, determined during the investigation, FDA may restrict its administrative actions to the IRB or to a component of the parent institution determined to be responsible for formal designation of the IRB.	(whether or not the research was subject to federal regulation).
56.121 Disqualification of an IRB or an institution ...The Commissioner may disqualify an IRB or the parent institution if the Commissioner determines that: 1. The IRB has refused or repeatedly failed to comply with any of the regulations set forth in this part, and 2. The non-compliance adversely affects the rights or welfare of the human subjects in a clinical investigation....	46.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency The department or agency head will evaluate all applications and proposals involving human subjects.... This evaluation will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained. On the basis of this evaluation, the department or agency head may approve or disapprove the application or proposal, or enter into negotiations to develop an approvable one. 46.122 Use of Federal Funds Federal Funds administered by a department or agency may not be expended for research involving human subjects unless the requirements of this policy have been satisfied.
56.122 Public disclosure of information regarding revocation A determination that the FDA has disqualified an institution and the administrative record regarding that determination are disclosable to the public under part 20. 56.123 Reinstatement of an IRB or an institution An IRB or an institution may be reinstated if the Commissioner determines...that the IRB or institution has provided adequate assurance that it will operate in compliance with the standards set forth in this part....	No comparable provisions.
56.124 Actions alternative or additional to disqualification Disqualification of an IRB...is independent of...other proceedings or actions authorized by the Act. The FDA may, at any time, through the Department of Justice institute any appropriate judicial proceedings (civil or criminal) and any other appropriate regulatory action, in addition to or in lieu of, and before, at the time of or after disqualification. The agency may also refer pertinent matters to another Federal, State, or local government agency for	46.124 Conditions With respect to any research project...the department...head may impose additional conditions prior to or at the time of approval when in the judgment of the department or agency head additional conditions are necessary for the protection of human subjects.

FDA Regulations	HHS Regulations
any action that that agency determines to be appropriate.	
50.20 and 46.116 General requirements for informed consent are virtually identical.	
50.25 and 46.116(a) Elements of informed consent are virtually identical except: ○ 50.25(a)(5) requires the confidentiality statement to note "the possibility that the FDA may inspect the records." ○ 46.116(a)(5) discusses the requirement of key information that must be presented at the beginning of the consent form. ○ 46.116(e) and (f) state the conditions under which the IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirement to obtain informed consent [the conditions could not apply in FDA regulated research]	
50.27 and 46.117 Documentation of informed consent are virtually identical except: • 46.117(c)(1) is not included in FDA's comparative section contained in 56.109(c). 46.117(c)(1) allows the IRB to waive the requirement for the investigator to obtain a signed consent form if it finds that the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.	
50.23(a)-(c) Exception from general requirements Describes an exception from the general requirements for obtaining informed consent in circumstances that are life-threatening; informed consent cannot be obtained from the subject; time is not sufficient to obtain consent from the subject's legal representative; and there is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.	No comparable provisions
50.23(d) Waiver of informed consent for military personnel Describes the criteria and standards that the President is to apply in making a determination that informed consent is not feasible or is contrary to the best interests of the individual in military exigencies in accordance with the Strom Thurmond Defense Authorization Act for FY 1999	No comparable provision.

1. *In 1991 FDA's regulations were harmonized with the common rule to the extent permitted by statute.*
2. *Differences in the rules are due to differences in the statutory (1) scope or (2) requirements.*
3. *FDA has additional IRB requirements contained in parts 312, 812, and 814. For example, 812.2(b)(ii) states that research is considered to have an approved application for an IDE, unless FDA has notified the sponsor to the contrary, if IRB approval of the investigation is obtained after presenting the reviewing IRB with a brief explanation of why the device is not a significant*

risk, and maintains such approval, (iii) and ensures informed consent is obtained in accordance with part 50.

4. *HHS has special subparts relating to vulnerable populations, e.g., children, prisoners, pregnant women, etc. FDA does not have comparable provisions for these populations.*
5. *The HHS regulations require assurances and certifications from the grantee institution. FDA regulations generally require assurances of compliance from either or both the sponsor of the research and the clinical investigator.*

Appendix 9: Inclusion of Women and Minorities in Study Populations: Guidance for IRBs and Principal Investigators

The principle of Justice as outlined in the Belmont Report requires that research subjects be treated fairly. For example, subjects should be carefully and equitably chosen to ensure that certain individuals, or classes of individuals are not systematically selected or excluded, unless there are scientifically or ethically valid reasons for doing so.

Consistent with this principle, the NIH Revitalization Act of 1993 legislated that special attention be given to the inclusion of women and minority groups in all clinical research conducted or supported by the NIH.

On March 9, 1994, the NIH issued Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research (copy available from OHSR). These Guidelines focus on the requirement for appropriate representation of women and minority groups in all NIH-supported or -conducted clinical research, particularly in Phase III clinical trials. On August 2, 2000, the NIH updated the Guidelines to reflect the requirement to include in the research plan of Phase III trials a description of how valid analyses will be conducted to detect significant differences in intervention effect among different populations. To review the update, see https://grants.nih.gov/policy/inclusion/women-and-minorities.htm. Even though most Intramural Research Program (IRP) clinical research does not consist of Phase III clinical trials, the Guidelines nevertheless direct that all IRP clinical research projects should strive to recruit and enroll the most diverse study population consistent with the purpose of the project.

The Guidelines contain the following policy statements:

"It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification establishes to the satisfaction of the relevant Institute or Center Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Exclusion under other circumstances may be made by the Director, NIH, upon the recommendation of an Institute/Center Director based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be routinely excluded from participation in clinical research. All NIH-supported biomedical and behavioral research involving human subjects is defined as clinical research. This policy applies to research subjects of all ages."

"The inclusion of women and members of minority groups and their subpopulations must be addressed in developing a research design appropriate to the scientific objectives of the study. The research plan should describe the composition of the proposed study population in terms of gender and racial/ethnic group, and provide a rationale for selection for such subjects. Such a plan should contain a description of the proposed outreach programs for recruiting women and minorities as participants."

Appendix 10: NIH Policy and Guidelines on the Inclusion of Children as Participants in Research involving Human Subjects

Inclusion of Children in Clinical Research: Change in NIH Definition
Notice Number: NOT-OD-16-010
Release Date: October 13, 2015
Issued by National Institutes of Health (NIH)

Purpose

The purpose of this notice is to notify NIH applicants/offerors and grantees/contractors about a change related to the NIH policy on the inclusion of children in clinical research. NIH's long-standing policy has been that children must be included in all human subjects' research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them. The policy was developed because medical treatments applied to children are often based upon testing done only in adults, and scientifically evaluated treatments are less available to children due to barriers to their inclusion in research studies. Therefore, applicants/offerors conducting human subjects' research must include a description of plans for including children. If children (or a subset of children) will be excluded from the research, the application or proposal must present an acceptable justification.

What's Changing: Starting with applications/proposals submitted for due dates on or after January 25, 2016, for the purposes of inclusion policy, the age of a child will be defined as individuals under 18 years old instead of under 21 years old, the current NIH definition of a child for inclusion policy considerations. Applicants/offerors for NIH funding will still be expected to justify the age range of the proposed participants in their clinical research, with particular attention paid to addressing the inclusion (or exclusion) of children (or subsets of children). However, now that threshold applies to individuals under the age of 18 rather than under the age of 21.

Reason for Change: Consideration of children as a vulnerable population for human protections from research risk and the NIH child inclusion policy are often conflated. While these are distinct policies, many think of children as under 18 years of age, typically the age of consent. This has sometimes led to confusion on the part of applicants/offerors, peer reviewers, grantees/contractors, and even NIH staff about how to ensure compliance with the child inclusion policy. By aligning the NIH definition for the age of a child with the typical age of consent and the common perception of the age of adulthood, the NIH can continue to implement this policy in a manner that focuses on the group of children that need particular attention.

The NIH recognizes that development continues well beyond 18 (and even 21, the current age); however, there is particular concern about ensuring the appropriate inclusion of individuals under 18 while also safeguarding this vulnerable group. NIH policies on inclusion are aimed at ensuring that appropriate individuals are included in clinical research and clinical trials. Results need to be generalizable to individuals that comprise

the population under study. This includes consideration of age as a factor in the scientific design.

NIH Policy and Guidelines on the Inclusion of Children as Participants in Research involving Human Subjects
Release Date: March 6, 1998

National Institutes of Health

SUMMARY: With this notice, the National Institutes of Health (NIH) establishes guidelines on the inclusion of children in research involving human subjects, including, but not limited to, clinical trials, supported or conducted by the NIH.

EFFECTIVE DATE: This policy applies to all initial (Type 1) applications/ proposals and intramural projects submitted for receipt dates after October 1, 1998.

I. Introduction

This document sets forth the policy and guidelines on the inclusion of children in research involving human subjects that is supported or conducted by the National Institutes of Health (NIH). The goal of this policy is to increase the participation of children in research so that adequate data will be developed to support the treatment modalities for disorders and conditions that affect adults and may also affect children. For the purposes of this NIH policy, studies involving human subjects include categories of research that would otherwise be exempted from the DHHS Policy for Protection of Human Research Subjects. These categories of research are exempted from the DHHS policy because they pose minimal risk to the participants, and not because the studies should not include children. Examples of such research include surveys, evaluation of educational interventions, and studies of existing data or specimens that should include children as participants. Nevertheless, the inclusion of children as participants in research must be in compliance with all applicable subparts of §45CFR46 as well as with other pertinent federal laws and regulations whether or not the research is otherwise exempted from §45CFR46.

II. Background

The policy was developed because medical treatments applied to children are often based upon testing done only in adults, and scientifically evaluated treatments are less available to children due to barriers to their inclusion in research studies. These concerns were specifically articulated in Congressional directives to the NIH as reflected in language from the FY 1996 House and Senate Appropriations Committee reports as follows:

HOUSE

The Committee is concerned that inadequate attention and resources are devoted to pediatric research conducted and supported by the National Institutes of Health. Most research on the cause, treatment and cure of diseases which affect children rely primarily on adults as subjects in clinical trials. Consequently, treatment options which may be effective for adults can have an adverse impact on the outcome of children as well as on their future growth and development. The Committee strongly encourages the NIH to strengthen its portfolio of basic, behavioral and clinical research conducted and supported by all of its relevant institutes, to establish priorities for pediatric research, and to ensure the adequacy of translational research from the laboratory to the clinical setting. The Committee encourages the NIH to establish guidelines to include children in clinical research trials conducted and supported by NIH. The Committee expects NIH to develop performance indicators to measure specific progress on the above, demonstrated by the development of new programs or strengthening of existing programs and to report to the Committee prior to the 1997 appropriations hearings (H.R. Report No. 209, 104th Congress, 1st session, 80-81, 1995).

SENATE

Pediatric research---The Committee recognizes the substantial benefits that biomedical research offers to the health and well-being of our Nation's children. Savings from productive innovations in health care, derived from scientific investigations of the highest quality, can be significant in terms of dollars and quality of life for children. The opportunities for advancements in the prevention and treatment of diseases which affect children or begin in childhood have never been greater. The Committee intends to work with the Office of the Director as it explores ways to take advantage of such opportunities and strengthen the NIH's capacity to support and encourage extramural pediatric research. Of particular interest is the establishment of guidelines to include children in clinical research trials conducted and supported by the NIH (S. Report No. 145, 104th Congress, 1st session, 112, 1995).

In June 1996, the National Institute of Child Health and Human Development (NICHD) and the American Academy of Pediatrics convened a workshop to address the inclusion of children as participants in research. After reviewing reports, background papers, and a study of a sample of NIH-sponsored clinical research abstracts that suggested that 10-20% inappropriately excluded children, the conveners concluded that there is a need to enhance the inclusion of children in clinical research. This conclusion is based upon scientific information, demonstrated human need, and considerations of justice for children in receiving adequately evaluated treatments. The need reaches

across a broad spectrum of clinical research, including studies on pharmaceutical and therapeutic agents, behavioral, developmental and life cycle issues including childhood antecedents of adult disease, and prevention and health services research.

The American Academy of Pediatrics has reported that only a small fraction of all drugs and biological products marketed in the U.S. have had clinical trials performed in pediatric patients and a majority of marketed drugs are not labeled for use in pediatric patients. Many drugs used in the treatment of both common childhood illnesses and more serious conditions carry little information in the labels about use in pediatric patients. In order to address these inadequacies, the Food and Drug Administration (FDA) has published (http://www.fda.gov) a proposed regulation calling for changes in the testing of prescription drugs to ensure that manufacturers specifically examine the drugs effects on children if the medications are to have clinically significant use in children.

In January 1997 the NIH announced (NIH Guide for Grants and Contracts, volume 26,Number 3, January 31, 1997) plans to develop a policy for the inclusion of children in NIH-supported human subject research. This publication fulfills the goal of the announced plan.

III. Policy

It is the policy of NIH that children (i.e., individuals under the age of 21) must be included in all human subjects research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them. This policy applies to all NIH conducted or supported research involving human subjects, including research that is otherwise "exempt" in accord with Sections 101(b) and 401(b) of §45CFR46 - Federal Policy for the Protection of Human Subjects. The inclusion of children as subjects in research must be in compliance with all applicable subparts of §45CFR46 as well as with other pertinent federal laws and regulations. Therefore, proposals for research involving human subjects must include a description of plans for including children. If children will be excluded from the research, the application or proposal must present an acceptable justification for the exclusion.

In the research plan, the investigator should create a section titled "Participation of Children". This section should provide either a description of the plans to include children and a rationale for selecting or excluding a specific age range of child, or an explanation of the reason(s) for excluding children as participants in the research. When children are included, the plan must also include a description of the expertise of the investigative team for dealing with children at the ages included, of the appropriateness of the available facilities to accommodate the children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to

the purpose of the study. Scientific review groups at the NIH will assess each application as being "acceptable" or "unacceptable" in regard to the age-appropriate inclusion or exclusion of children in the research project, in addition to evaluating the plans for conducting the research in accord with these provisions.

Justifications for Exclusions

It is expected that children will be included in all research involving human subjects unless one or more of the following exclusionary circumstances can be fully justified:

1. The research topic to be studied is irrelevant to children.

2. There are laws or regulations barring the inclusion of children in the research. For example, the regulations for protection of human subjects allow consenting adults to accept a higher level of risk than are permitted for children.

3. The knowledge being sought in the research is already available for children or will be obtained from another ongoing study, and an additional study will be redundant. Documentation of other studies justifying the exclusions should be provided. NIH program staff can be contacted for guidance on this issue if the information is not readily available.

4. A separate, age-specific study in children is warranted and preferable. Examples include:

   a. The relative rarity of the condition in children, as compared to adults (in that extraordinary effort would be needed to include children, although in rare diseases or disorders where the applicant has made a particular effort to assemble an adult population, the same effort would be expected to assemble a similar child population with the rare condition);

   b. The number of children is limited because the majority are already accessed by a nationwide pediatric disease research network, so that requiring inclusion of children in the proposed adult study would be both difficult and unnecessary (in that the topic was already being addressed in children by the network) as well as potentially counterproductive (in that fewer children could be available for the network study if other studies were required to recruit and include them);

   c. Issues of study design preclude direct applicability of hypotheses and/or interventions to both adults and children (including different cognitive,

developmental, or disease stages or different age-related metabolic processes). While this situation may represent a justification for excluding children in some instances, consideration should be given to taking these differences into account in the study design and expanding the hypotheses tested or the interventions to allow children to be included rather than excluding them.

5. Insufficient data are available in adults to judge potential risk in children (in which case one of the research objectives could be to obtain sufficient adult data to make this judgment). While children usually should not be the initial group to be involved in research studies, in some instances, the nature and seriousness of the illness may warrant their participation earlier based on careful risk and benefit analysis.

6. Study designs aimed at collecting additional data on pre-enrolled adult study participants (e.g., longitudinal follow-up studies that did not include data on children).

7. Other special cases justified by the investigator and found acceptable to the review group and the Institute Director.

IV. Implementation

A. Date of Implementation

This policy applies to all initial applications (Type 1)/proposals and intramural projects submitted for receipt dates after October 1, 1998.

B. Roles and Responsibilities

This policy applies to all NIH-conducted or -supported research involving human subjects. Certain individuals and groups have special roles and responsibilities with regard to the adoption and implementation of these guidelines.

1. Principal Investigators

Principal Investigators should assess the scientific rationale for inclusion of children in the context of the topic of the study. Questions that should be considered in developing a study involving human subjects may include, but are not limited to, the following: When is the exclusion of children appropriate? Under what circumstances is it appropriate? At what ages is it appropriate? The Principal Investigator should address the policy in the application, providing the required information on participation of children in research projects, and required justifications for any exceptions allowed under

the policy in the research plan under a section titled "Participation of Children".

2. Institutional Review Boards (IRBs)

The IRB addresses the appropriateness of the population studied in terms of the aims of the research and ethical standards. IRBs have the responsibility to examine ethical issues, including equitable selection of research participants in accordance with Federal Regulations (§45CFR46) The participation of children in research, including children of both genders and children from minority groups, is important to assure that they receive a share of the benefits of research. IRBs have special review requirements (§45CFR46, Subpart D, Sec. 401-409) to protect the well-being of children who participate in research. IRBs may approve research involving children only if the special provisions are met.

3. Scientific Review Groups

In conducting peer review of applications/proposals for scientific and technical merit, appropriately constituted scientific review groups, technical evaluation groups, and intramural review panels will evaluate the proposed plan for inclusion or exclusion of children as acceptable or unacceptable. Therefore, these groups must include appropriate expertise in research involving children to make the evaluation.

4. Institute/Center Obligations

Following scientific review and Council review, Institute/Center Directors and their staff shall determine whether: (a) the research involves human subjects, and (b) the inclusion or exclusion of children meets the requirements of the policy. Program staff should assess exceptions to this policy in view of the IC research portfolio.

5. Educational Outreach by NIH to Inform the Professional Community

NIH staff will present these guidelines to investigators, IRB members, peer review groups, and Advisory Councils in a variety of public forums.

6. Applicability to Foreign Research Involving Human Subjects

The policy of inclusion of children in NIH-conducted or supported research activities in foreign countries (including collaborative activities) is the same as that for research conducted in the U.S.

V. Definitions

For the purpose of implementing these guidelines, the following definitions apply.

A. Child

*For purposes of this policy, a child is an individual under the age of 21 years. ** (See newer guidance at the beginning of this Appendix).* This policy and definition do not affect the human subject protection regulations for research on children (§45CFR46) and their provisions for assent, permission, and consent, which remain unchanged.

It should be noted that the definition of child described above will pertain notwithstanding the FDA definition of a child as an individual from infancy to 16 years of age, and varying definitions employed by some states. Generally, State laws define what constitutes a "child," and such definitions dictate whether or not a person can legally consent to participate in a research study. However, State laws vary, and many do not address when a child can consent to participate in research. Federal Regulations (§45CFR46, subpart D, Sec.401-409) address DHHS protections for children who participate in research, and rely on State definitions of "child" for consent purposes. Consequently, the children included in this policy (persons under the age of 21) may differ in the age at which their own consent is required and sufficient to participate in research under State law. For example, some states consider a person age 18 to be an adult and therefore one who can provide consent without parental permission.

Additionally, IRBs have special review requirements to protect the well-being of children who participate in research. These requirements relate to risk, benefit, parental/guardian consent, and assent by children, and to research involving children who are wards of the State or of another institution. The local IRB approves research that satisfies the conditions set forth in the regulations.

B. Human Subjects

The definition of a human subject appears in Title 45 part 46 of the Department of Health and Human Services Regulations for the Protection of Human Subjects and is as follows: "Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains: (1) Data through intervention or interaction with the individual, or (2) identifiable private information."

VI. Decision Tree for Participation of Children in Research
The inclusion of children in research is a complex and challenging issue. Nonetheless, it also presents the opportunity for researchers to address the concern that treatment modalities used to treat children for many diseases and disorders are based on research conducted with adults. The linked "decision

tree" is intended to facilitate the determination of policy implementation by Principal Investigators and reviewers with regard to the inclusion of children in research involving human subjects.

VII. Additional Requirements for Research that Includes Children

The following chart summarizes the additional requirements under the DHHS Regulations §45CFR46, Subpart D based on the risks and benefits to children who participate in research:

Types of Research	**Requirements**
No greater than minimal risk	Assent of child and permission of at least one parent
Greater than minimal risk AND prospect of direct benefit	Assent of child and permission of at least one parent Anticipated benefit justifies the risk, AND Anticipated benefit is at least as favorable as that of alternative approaches.
Greater than minimal risk and no prospect of direct benefit	Assent of child and permission of both parents Only a minor increase over minimal risk Likely to yield generalizable knowledge about the child's disorder or condition that is of vital importance for the understanding or amelioration of the disorder or condition, AND The intervention or procedure presents experiences to the child that are reasonably commensurate with those in the child's actual or expected medical, dental, psychological, social, or educational situations
Any other research	Assent of child and permission of both parents IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, AND The Secretary approves, after consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following publication and public comment

VIII. NIH Contacts for More Information

The following senior extramural staff from the NIH Institutes and Centers may be contacted for further information about the policy and relevant Institute/Center programs:

Dr. Marvin Kalt
National Cancer Institute Executive Plaza North, Room 600C, 6130 Executive Boulevard, Bethesda, Maryland 20892. Tel: (301) 496-5147. e-mail: mk74s@nih.gov

Dr. Jack McLaughlin, National Eye Institute, Executive Plaza South, Room 350, 6120 Executive Boulevard, Bethesda, Maryland 20892. Tel: (301) 496-9110. e-mail: jm82p@nih.gov

Dr. Ron Geller, National Health, Lung and Blood Institute, Rockledge Center 2, Room 7100, 6701 Rockledge Drive, Bethesda, Maryland 20892. Tel: (301) 435-0260. e-mail: rg33k@nih.gov

Dr. Mark Guyer, National Human Genome Research Institute, Building 38A, Room 604, 38 Library Drive, Bethesda, Maryland 20892. Tel: (301) 402-5407. e-mail: mg25m@nih.gov

Dr. Miriam Kelty, National Institute on Aging, Gateway Building, Room 2C218F, 7201 Wisconsin Avenue, Bethesda, Maryland 20892. Tel: (301) 496-9322. e-mail: mk46u@nih.gov

Dr. Kenneth Warren, National Institute on Alcohol Abuse and Alcoholism, Room 409, MSC 7003, 6000 Executive Boulevard, Bethesda, Maryland 20892-7003. Tel: (301) 443-4375. e-mail: kw46m@nih.gov

Dr. John McGowan, National Institute of Allergy and Infectious Diseases, Solar Building, Room 3C20, 6003 Executive Boulevard, Bethesda, Maryland 20892. Tel: (301) 496-7291. e-mail: jm80c@nih.gov

Dr. Steven Hausman, National Institute of Arthritis and Musculoskeletal and Skin Diseases, Building 31, Room 4C32, 31 Center Drive, Bethesda, Maryland 20892. Tel: (301) 402-1691. e-mail: sh41g@nih.gov

Dr. Yvonne Maddox, National Institute of Child Health and Human Development, Building 31, Room 2A03, 31 Center Drive, Bethesda, Maryland 20892. Tel: (301) 496-1848. e-mail: ym16x@nih.gov

Dr. Craig Jordan, National Institute of Deafness and Other Communication Disorders, Executive Plaza South, Room 400C, 6120 Executive Boulevard, Bethesda, Maryland 20892. Tel: (301) 496-8693. e-mail: cj34b@nih.gov

Dr. Lois Cohen, National Institute on Dental Research, Building 45, Room 4AN18E, 45 Center Drive, Bethesda, Maryland 20892. Tel: (301) 594-7710. e-mail: lc85n@nih.gov

Dr. Walter Stolz, National Institute of Diabetes and Digestive and Kidney Diseases, Building 45, Room 6AS25C, 45 Center Drive, MSC 6600, Bethesda, Maryland 20892-6600. Tel: (301) 594-8834. e-mail: ws23e@nih.go

Dr. Teresa Levitin, National Institute on Drug Abuse, Parklawn Building, Room 10-42, 5600 Fishers Lane, Rockville, Maryland 20857. Tel (301) 443-2755. e-mail:tl25u@nih.gov

Dr. Anne Sassaman, National Institute of Environmental Health Sciences, Building 3, Room 301, P.O. Box 12233, Research Triangle Park, North Carolina, 27709. Tel: (919) 541-7723. e-mail: as56j@nih.gov

Dr. Sue Shafer, National Institute of General Medical Sciences, Building 45, Room 2AN32D, 45 Center Drive, MSC 6200, Bethesda, Maryland, 20892-6200. Tel: (301) 594-4499. e-mail: ss78v@nih.gov

Dr. Richard Nakamura, National Institute of Mental Health, Parklawn Building, Room 17C-26, 5600 Fishers Lane, Rockville, Maryland 20857. Tel: (301) 443-4335. e-mail: rn3p@nih.gov

Dr. Constance Atwell, National Institute of Neurological Disorders and Stroke, Federal Building, Room 1016, 7550 Wisconsin Avenue, Bethesda, Maryland 20892. Tel: (301) 496-9248. e-mail: ca23c@nih.gov

Dr. Mary Leveck, National Institute of Nursing Research, Building 45, Room 3AN12, 45 Center Drive, MSC 6300, Bethesda, Maryland, 20892-6300. Tel: (301) 594-5963. e-mail: ml118t@nih.gov

Dr. Louise Ramm, National Center for Research Resources, Building 31, Room 3B11, 31 Center Drive, Bethesda, Maryland 20892. Tel: (301) 496-6023. e-mail: lr34m@nih.gov

Dr. Kenneth Bridbord, Fogarty International Center, Building 31, Room B2C39, 31 Center Drive, Bethesda, Maryland 20892. Tel: (301) 496-2516. e-mail: kb16r@nih.gov

Appendix 11: Phlebotomy Services for Research Purposes

It is Georgia Institute of Technology IRB policy that human blood for research purposes shall not be collected by untrained faculty, staff or students, but shall be drawn by trained phlebotomists at Stamps Health Services (Student Health), at Concentra Health Services, or within the research laboratory by an IRB approved trained professional.

Any exception to this policy must have Institutional Review Board approval from the Office of Research Integrity Assurance. Some examples qualifying for an exception include (1) blood is drawn at another research site and shipped to Georgia Tech for research/analysis; (2) the drawing of blood by physician researchers; (3) blood drawn in a clinical setting by personnel trained and supervised by a physician such that the physician's malpractice insurance covers the activity; and (4) having a trained phlebotomist on staff to perform blood draws within the research laboratory.

A. Stamps Health Services Laboratory Research Phlebotomy Protocol When GT Students Are Research Subjects

Stamps Health Laboratory Services has contracted to perform phlebotomy services for the Research activities and their donors at Georgia Institute of Technology. The Laboratory staff will be available to conduct such draws as pre-arranged by scheduling. Researchers must have a current Institutional Review Board (IRB)-approved protocol in order to utilize these services, and blood donors must be enrolled students with Georgia Tech-issued identification. This policy is written to aid in the delivery of IRB (Institutional Review Board) mandated research curriculum.

1. Specimen Collection and Transport:

- Scheduling:
  - On weekdays when the campus is open, SHS Laboratory offers phlebotomy services for research purposes beginning at 9AM and ending no later than 3:30 pm, EST.
  - Time blocks must be reserved no later than the day before the anticipated draw(s).
    - A 2-3 day advance notice is preferable.
    - Call 404 / 894-1424 to schedule a phlebotomy appointment.
  - When scheduling a draw, the Researcher shall provide the number of donors and volume of blood to be drawn from each donor.
    - All time blocks are scheduled on a first class basis.

        - No double booking is allowed.
    - If a scheduled phlebotomy is delayed by the researcher by more than 10 minutes, it will be the responsibility of the researcher to reschedule the draw if the following time slots are full.
    - The Researcher is responsible for transporting the collected specimen to its proper location.

2. Authorized Donors:

- Donors must be accompanied to the SHS Laboratory by a member of the research team named in the IRB protocol.
- All donors must be currently active Georgia Tech students. Students must present GT-issued identification.
- Donors must present to the SHS laboratory personnel a copy of their signed, IRB-approved and date-stamped consent form. (In cases where a waiver of documentation of consent has been approved, students will not be required to put their names on the IRB consent document. Such waivers will be indicated in the letter of IRB approval)

3. Materials and Supplies:

- The researcher must provide the necessary supplies for each blood draw: tubes, needles, syringes, Georgia Tech Environmental Health & Safety-approved transport carrier, etc.

4. Procedure:

- Responsibilities of the Researcher Requesting Phlebotomy Services
    - When setting up blood draws for a new IRB protocol, the researcher, research assistant, or designated representative ("researcher") must provide the Stamps Health Services laboratory with *copies of the IRB letter of approval and the IRB-approved and date-stamped consent form.*
    - Consent forms must list exclusionary criteria
        - Current pregnancy
        - History of immunodeficiency or HIV infection
        - History of allergy to latex
        - Blood Donation of 500 mls of whole blood during the immediate past 8-week period
        - Weight less than 15 kg regardless of age
        - Suspected anemia

- A copy of the donor's signed consent form must be presented to the SHS Laboratory personnel at the blood draw appointment.
- The researcher named in the IRB protocol must accompany donors to the SHS Laboratory.

- It is the responsibility of the researcher to adequately prepare the syringes and/or tubes for use.
- It is the responsibility of the researcher to transfer the collected sample to the appropriate vial if needed.
- It is the responsibility of the researcher adequately store, label, designate and transport the collected specimens from the SHS laboratory phlebotomy area to the research facility in an approved container.
- It is the responsibility of the researcher to track volume drawn from each donor to prevent excessive sampling from the same donor within an 8-week period.
  - **NOTE: No more than 500 mls. of whole blood can be obtained from any donor during an 8-week period.**
- SHS Laboratory will maintain a copy of the signed consent form and a confidential log of donor information and eligibility to participate in the IRB approved study, date and time of phlebotomy, and blood volume drawn.

5. Special procedural notes:

- Student Health Service patients are the first priority and as such may take precedence over a scheduled research phlebotomy. In this case, no time penalty will be incurred, and every effort will be made with available personnel to accommodate all.

All new researchers must provide a copy of the IRB approved research protocol to the SHS lab first before phlebotomy is scheduled.

B. Phlebotomy Services at Concentra Health Services for Georgia Tech Research Purposes

Researchers needing professional phlebotomy services *for human subjects who are NOT enrolled Georgia Tech students* may contact Concentra Health Services for assistance. (The Stamps Health Services Laboratory provides phlebotomy services for enrolled Georgia Tech students). Located at 688 Spring Street, Concentra Health Services is the current Occupational Health Program medical provider for Georgia Tech.

1. Scheduling:

- To schedule blood draws, call the Concentra Center Administrator at 404 / 881-1155, preferably 48 hours in advance. Researchers are encouraged to schedule small groups of draws together.

2. Responsibilities of the Researcher Requesting Phlebotomy Services:

- When setting up blood draws for a new IRB protocol, the researcher, research assistant, or designated representative ("researcher") must provide the Concentra Health Services laboratory with *copies of the IRB letter of approval and the IRB-approved and date-stamped consent form.*
    - Consent forms must list exclusionary criteria, such as:
        - Current pregnancy
        - History of immunodeficiency or HIV infection
        - History of allergy to latex
        - Blood donation of 550 ml. of whole blood during the immediate past 8 week period
        - Weight less than 110 lb. regardless of age
        - Suspected anemia
- *A copy of the donor's signed consent form must be presented to the Concentra Health Services Laboratory personnel at the blood draw appointment.* (When a waiver of documentation of consent has been approved, subjects will not be required to put their names on the IRB consent document. Waivers will be noted in the IRB approval letter).
- The researcher must provide a Georgia Tech Environmental Health & Safety-approved transport carrier.
- It is the responsibility of the researcher to adequately store, label, designate and transport the filled syringe and/or tube from Concentra Health Services laboratory phlebotomy area to the research facility in an approved container.
- It is the responsibility of the researcher to track volume drawn from each donor to prevent excessive sampling from the same donor within an 8 week period. *No more than 500 ml. of whole blood can be obtained from any donor during an 8 week period.*

3. Donors:

- Donors must be accompanied to Concentra Health Services by a member of the research team named in the IRB protocol.
- Donors must complete a routine Concentra Health Services "Consent to Treat" form.

- Donors must also bring a copy of their *signed, IRB-approved and date-stamped consent form.*

C. Phlebotomy Services in the Research Laboratory for Georgia Tech Research Purposes

All research laboratories performing in-lab blood draws **must comply** with the **CDC Guidelines for Infection Control:** https://www.cdc.gov/covid/?CDC_AAref_Val=https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control.html.

All research laboratories handling human blood samples **must** adhere to **Standard Precautions:** https://www.cdc.gov/infection-control/hcp/basics/standard-precautions.html?CDC_AAref_Val=https://www.cdc.gov/infectioncontrol/basics/standard-precautions.html .

In order for blood draws to be performed in the research laboratory, there are three options available:

Option 1 - Hire a certified phlebotomist.
Option 2 - Send employees to local phlebotomy certification training to support research phlebotomy needs.
Option 3 - Research a certified phlebotomist to go and train the researcher at the research location. (An option might be for the Stamps Medical Technician to do the training).

All persons conducting phlebotomy must have currently valid Red Cross First Aid Certification or relevant professional education in managing adverse events associated with phlebotomy such as hematoma, hemorrhage, syncope, or nausea and Blood Borne Pathogen Training from EH&S. *Phlebotomy certification through ASCP (American Society for Clinical Pathology), ASPT (American Society of Phlebotomy Technicians), NCA (National Credentialing Agency for Laboratory Personnel), or equivalent.

Appendix 12: Data Use Agreements

A Data Use Agreement (DUA; also known as a Data Transfer & Use Agreement or DTUA) is a contract used for the transfer of data that has been developed by nonprofit, government or private industry, where the data is nonpublic or is otherwise subject to some restrictions on its use. The data may be needed as a necessary component of a research project. It may or may not be human subject data from a clinical trial, or a Limited Data Set as defined in HIPAA.

Universities want to ensure that DUA terms protect confidentiality when necessary but permit appropriate publication and sharing of research results in accordance with University policies, applicable laws and regulations, and federal requirements.

Georgia Tech is a state-related entity that receives a large proportion of its research funding from the U.S. federal government. In order to ensure that DUAs meet Institute policies as well as the requirements of funding agencies, the Office of Sponsored Programs' Exchange Agreements team will review DUA requests and handle the negotiation and signature of DUAs.

Appendix 13: Enrolling Oneself in One's Own Study – "Self-Experimentation"

Some researchers may want to participate in their own studies, a practice known as "self-experimentation." The federal regulations are silent on this point, making no distinction between self-experimentation and participation by others. The Institutional Review Board requires that such self-experimentation be fully described in a protocol that is submitted for IRB review.

This policy (1) may protect researchers from unwarranted risks and (2) allows a neutral third party to raise concerns, if any, regarding credibility of resulting data.

Appendix 14: Sample Site Permission Letter

When researchers will be conducting research or recruiting subjects at an off-campus site, written permission may be required from the site manager. Sample site permission letters are provided here:

School Letterhead

Date

Dr. Principal Investigator
School of X
Georgia Institute of Technology
Atlanta, GA 30332 –XXXX

Dear Dr. Investigator:

This is to confirm that THIS SCHOOL authorizes you to conduct data collection/recruitment/follow-up activities with our students on Month Day Year in accordance with the research protocol, "TITLE."

Sincerely,
School Principal or District Superintendent

Company Letterhead

Date

Dr. Principal Investigator
School of X
Georgia Institute of Technology
Atlanta, GA 30332 –XXXX

Dear Dr. Investigator:

This is to confirm that THIS COMPANY authorizes you to conduct data collection/recruitment/follow-up activities at our SPECIFIC SITE(S) on Month Day Year in accordance with the research protocol, "TITLE."

Sincerely,
President of THIS COMPANY

Appendix 15: Additional Requirements for Research Involving Department of Defense, Incorporated by Addenda to Federalwide Assurance

An Addendum to Georgia Tech's Federalwide Assurance incorporates the Department of Defense's (DoD) additional requirements for human subjects research involving the DoD. Human subjects research involves the DoD when any of the following apply:

- The research is conducted by or in part by the DoD.
  - Research involving human subjects that is performed by DoD personnel.
- The research is supported by the DoD.
  - Research involving human subjects for which the Department of Defense is providing at least some of the resources. Resources may include but are not limited to funding, facilities, equipment, personnel (investigators or other personnel performing tasks identified in the research protocol), access to or information about DoD personnel for recruitment, or identifiable data or specimens from living individuals. It includes both DoD-conducted research involving human subjects (intramural research) and research conducted by a non-DoD institution.

A. Human Subjects Research as Defined by the DoD

Except as detailed in §32CFR219.104, this policy applies to all research involving human subjects conducted, supported, or otherwise subject to regulation by any Federal department or agency that takes appropriate administrative action to make the policy applicable to such research (§32CFR219.101).

- Human Subject (§32CFR219.102)
  1. Human subject means a living individual about whom an investigator (whether professional or student) conducting research:
     i. Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.
  2. Intervention includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

3. Interaction includes communication or interpersonal contact between investigator and subject.
4. Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).
5. Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
6. An identifiable biospecimen is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

- Research (§32CFR219.102)
    - Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:
        1. Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
        2. Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated

with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

3. Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
4. Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

B. Specific DoD Requirements

The DoD requirements, which comport with DoDI 3216.02 and include those that are component-specific, are described below. (These additional requirements do not apply when DoD personnel incidentally participate as subjects in research that is not supported by DoD).

1. EDUCATION

Investigators and all members of the research team must satisfy research ethics education initially and on a continuing basis [DoDI 3216.02].

- **Air Force Research Laboratory (AFRL)**

The Air Force Research Laboratory requires initial and recurrent training in the protections of human subjects for all personnel named in the protocol. Non-DoD personnel acting under a non-DoD Assurance are required to complete training prior to three years from the date of the previous training. Initial and recurrent training for investigators will consist of the designated AFRL modules on the Collaborative Institutional Training Initiative (CITI) web site. *The Air Force will accept Georgia Tech's regular CITI modules, in lieu of the Air Force modules, for undergraduate researchers. If substituted for the AF modules, the Georgia Tech CITI modules must also be completed every three years.* [AFRLI 40-402]

- **Department of the Army**

The US Army Medical Research & Materiel Command (AMRMC) *Guidelines for Investigators* state: *"Before conducting human subjects research, the investigators and key study personnel must complete human research protection training in accordance with their institution's requirements. Principal and Co-Investigators must submit documentation of the most recent human research protection training to the HRPO as part of the submission package for the protocol. Training may also be requested for other research personnel with significant interaction with research*

volunteers. The HRPO requires that human research protection training be successfully completed within the last three years. In addition, for all investigational drug and device protocols, successful completion of a course in the conduct of clinical research in accordance with Good Clinical Practices (GCP) is recommended for all investigators." [United States Army Medical Research and Materiel Command (USAMRMC) Policy #2010-33, Requirements for Initial and Ongoing Education and Training in the Protection of Human Subjects in Research, dated 10 December]

The US Army Research Development & Engineering Command (ARDEC) requires that training be completed initially and every two years.

For sponsors other than USAMRMC and ARDEC, contact the Army program officer for specific information about specific education requirements.

• **Department of Navy (DON)**
DON requires initial and recurrent training by all investigators every three years. The DON will accept Georgia Tech's human subjects research CITI training modules, in lieu of the DON modules. [SECNAVINST 3900.39E]

• **Office of the Secretary of Defense for Personnel and Readiness**
Initial and annual training is required for all investigators, per HA Policy 05-003.

The Georgia Tech IRB will accept completion of any DOD-mandated CITI modules as sufficient and will not also require completion of the Ga Tech CITI modules. Personnel completing the DOD CITI modules will need to forward their CITI certificates to the Office of Research Integrity Assurance via email to irb@gatech.edu.

Georgia Tech requires completion of CITI refresher modules every three years. The Office of Research Integrity Assurance will assist those needing to meet an agency-imposed requirement for more frequent training.

2. SCIENTIFIC REVIEW
The Department of Defense requires that new research and substantive amendments to approved research must undergo review for scientific merit prior to ethics (IRB) review, and that review must be considered by the IRB. A sample scientific merit review form that may be used for this purpose is attached as Appendix 16 to these *Policies & Procedures*. [DoDI 3216.02]

3. ACTIVE DUTY MILITARY--PROTECTIONS AGAINST UNDUE INFLUENCE

Additional protections for military research subjects are in place to minimize undue influence. These include the following: Officers are not permitted to influence the decision of their subordinates; officers and senior non-commissioned officers may not be present at the time of recruitment; officers and senior noncommissioned officers have a separate opportunity to participate; and when recruitment involves a percentage of a unit, an independent ombudsman is present. [DoDI 3216.02]

4. PROVISIONS FOR RESEARCH-RELATED INJURY

Investigators must explain to subjects any provisions for medical care for research-related injury, and such provisions, if any, must be described in the consent process and document. [DoDI 3216.02]

5. REPORTING UNANTICIPATED PROBLEMS INVOLVING RISK TO SUBJECTS AND OTHERS (UPIRTSOs), INCLUDING ADVERSE EVENTS, AND RESEARCH RELATED INJURY

Report unanticipated problems, adverse events, research-related injury and suspensions or terminations of research. These problems and events must be reported in a timely manner to the Assistant Secretary of Defense for Research and Engineering (ASD(R&E)) and to the Georgia Tech Office of Research Integrity Assurance. [DoDI 3216.02]

6. RESEARCH MONITOR

A research monitor shall be appointed by name when appropriate for studies involving more than minimal risk to subjects. Additionally, the research monitor may be identified by an investigator or appointed by an IRB or IO for research involving human subjects determined to involve minimal risk. There may be more than one research monitor (e.g., if different skills or experiences are necessary). The monitor may be an ombudsman or a member of the data safety monitoring board. [DoDI 3216.02]

The duties of the research monitor shall be determined on the basis of specific risks or concerns about the research. The research monitor may perform oversight functions (e.g., observe recruitment, enrollment procedures, and the consent process for individuals, groups or units; oversee study interventions and interactions; review monitoring plans and UPIRTSO reports; and oversee data matching, data collection, and analysis) and report their observations and findings to the IRB or a designated official. [DoDI 3216.02]

The research monitor may discuss the research protocol with the investigators, interview human subjects, and consult with others outside of the study about the research. The research monitor shall have authority to stop a research protocol in progress, remove individual human subjects from a research protocol, and take whatever steps are necessary to protect the safety and well-being of human subjects until the IRB can assess the monitor's report. [DoDI

3216.02]Research monitors shall have the responsibility to promptly report their observations and findings to the IRB or other designated official.

The IRB must approve a written summary of the monitors' duties, authorities, and responsibilities. The IRB or HRPP official shall communicate with research monitors to confirm their duties, authorities, and responsibilities. [DoDI 3216.02]

The research monitors shall have expertise consonant with the nature of risk(s) identified within the research protocol, and they shall be independent of the team conducting the research involving human subjects. [DoDI 3216.02]

- **Department of the Air Force [AFRLI 40-402]**
  In addition to the requirements under DoDI 3216.02, the duties of a Research Monitor include:

  - Determining, with the concurrence of the IRB, the level of on-site research observation that is required for the level and type of risk(s). Depending on the nature of the risks involved during the experiment, a research observer may be required to be on call, in the same building, or continuously present and in communication with the subject.

  - If research requires on-scene observation, and the research monitor is not required to personally provide this observation, but the research monitor is responsible to design an appropriate system to provide observation, and with the IRB must concur/approve. This includes selection and training of any research observer.

  - Ensuring a mechanism exists that informs subjects of the advocacy role of research monitors and delineates a process by which subjects may contact the overall Research Monitor should they desire to do so.

  - Reporting to the IRB and Department/Division Chief any adverse event involving a subject. Any research/ consultant should assist in determining actual or potential harm. The report should include the research monitor’s recommendation as AFRLI40-402 21 APRIL 2016 21 to whether or not the protocol should be stopped pending further investigation or until the IRB can access the research monitor’s report.

- Any medical research consultant will be credentialed or licensed as appropriate to the medical risks involved in the research.

7. ADDITIONAL SAFEGUARDS FOR RESEARCH CONDUCTED WITH INTERNATIONAL POPULATIONS

Special protections are required when research is proposed to be conducted with international populations. Research *that is conducted outside the United States and its territories and possessions* must also comply with applicable requirements of the foreign country and its national laws and requirements. [DoDI 3216.02]

• Department of the Air Force

The Air Force requires that human use research that is to be conducted in a country other than the United States must be reviewed and approved by an IRB or similar body in the country where the research will take place. Whenever possible, this committee should satisfy the IRB membership requirements outlined in 32 CFR 219.107. This IRB or ethics committee must be able to review the research and ensure that it is acceptable based on national and local requirements, standards, and norms. This committee must also be willing to serve in an oversight capacity to assist the AFRL IRB in any matters of compliance and oversight. The AFRL IRB must be provided with the informed consent documents in the native language, as well as a back-translated version for review. All international research, regardless of risk level or determination of exemption, must be reviewed and approved by AFMSA/SGE-C prior to research commencement. [AFRLI 40-402]

8. WAIVER OF CONSENT

• Uniform Service Code

Funds appropriated to the Department of Defense may not be used for research involving a human being as an experimental subject unless (1) the informed consent of the subject is obtained in advance; or (2) in the case of research intended to be beneficial to the subject, the informed consent of the subject or a legal representative of the subject is obtained in advance. The Secretary of Defense may waive the prohibition in this section with respect to a specific research project to advance the development of a medical product necessary to the armed forces if the research project may directly benefit the subject and is carried out in accordance with all other applicable laws. [10 USC 980]

• Department of Defense (DoD)

If the research involves interventions or interactions with subjects, a waiver of consent or parental permission requires approval from the Secretary of Defense or the delegated Heads of the OSD and DoD

Components. If the research participant does not meet the definition of experimental subject, the IRB may provide a waiver of consent, if appropriate. [DoDI 3216.02]

• Department of Navy (DON)
Requests for waiver shall not be made directly to ASD (R&E), but should be coordinated through the DON institution supporting the research and the Director, DON HRPP. The Navy SG will review and, if appropriate, forward requests for waiver to the Secretary of the Navy (SECNAV). [SECNAVINST 3900.39E].

9. RESEARCH INVOLVING MINORS

Research involving human subjects conducted or supported by the Department of Defense that recruits children to be subjects must meet the additional relevant protections of subpart D of §45 CFR 46 unless otherwise modified by the DoD Instruction. [DoDI 3216.02]

• Department of the Army [AR 70-25]
Minors may participate as subjects when the following conditions are met:

1. The research is intended to benefit the subject, and any risk involved is justified by the expected benefit to the minor
2. The expected benefits are at least as favorable to the minor as those presented by available alternatives.
3. A legally authorized representative has been fully informed and voluntarily consents, in advance, for the minor to participate in the research.
4. The minor, if capable, has assented in writing. In determining whether the minor is capable of assenting, the HUC will consider the minor's age, maturity, and psychological state. The HUC may waive assent for some or all minors involved in the study if it determines that the:
    a. Capability of some or all of the minors is so limited that they cannot be reasonably consulted, or
    b. Procedure involved in the research holds out a prospect for direct benefit that is important to the health or well-being of the minor, and is available only in the context of research.

10. LIMITATIONS ON COMPENSATION FOR U. S. MILITARY PERSONNEL

The Dual Compensation Act prohibits an individual from receiving pay from more than one position for more than an aggregate of 40 hours of work in one calendar week. These limitations include limitation on dual compensation,

which prohibit an individual from receiving pay or compensation for research during duty hours and US military personnel may be compensated for research if the participant is involved in the research when not on duty. This prohibition applies to employees paid from either appropriated or non-appropriated funds, or a combination thereof, and includes temporary, part-time, and intermittent appointments. This law is not applicable to enlisted off-duty military personnel in relation to their military duty. [Dual Compensation Act and 24 U.S.C. 30]

- **Active Duty Federal Personnel**

  Active duty federal personnel may receive up to $50 per blood draw. However, active duty federal personnel cannot be compensated for general research participation other than blood draws. [DoDI 3216.02]

- **Off-Duty Federal Personnel**

  Off-duty federal personnel may receive up to $50 per blood draw. If the blood draw research is not federally funded, then the off-duty personnel may be compensated in a reasonable amount as approved by the IRB. Additionally, off-duty personnel may be compensated for general research in a reasonable amount as approved by the IRB. However, this compensation cannot come directly from a federal source. [DoDI 3216.02]

- **Non-Federal Personnel**

  Non-federal personnel may receive up to $50 per blood draw in DoD-funded research. Additionally, non-federal personnel may be compensated for general research in a reasonable amount as approved by the IRB. These funds can come directly from either federal or non-federal sources. [DoDI 3216.02]

11. SURVEY RESEARCH

Research involving the administration of surveys to, or interviews of, DoD personnel (military or civilian) may require DoD approval of the surveys or interview questions. This involves research where DoD personnel and civilian personnel (working with the DoD and/or spouses and family members of DoD personnel) are asked to complete surveys; not when researchers funded by the DoD are conducting surveys of non-DoD personnel. For instructions on surveying military personnel across branches of the Department of Defense, see DoDI 1100.13 at https://www.esd.whs.mil/Portals/54/Documents/DD/issuances/dodi/110013p.pdf.

12. DRUGS, DEVICES AND BIOLOGICS, INVESTIGATIONAL TEST ARTICLES

Research involving human subjects using surveys, materials under the purview of the FDA, or individually identifiable health information may be subject to additional Federal or DoD requirements, such as those identified under 21 CFR 50, 56, 312, 600 and 812 (DoDI 3216.02). If your research is considered to be "an organized program of healthcare preventive therapeutic treatment, or preparations for such treatment, designed to meet the actual, anticipated, or potential needs of a group of military personnel in relation to military mission" (Force Health Protection Program), then additional regulations may apply under DoDI 6200.02.

• Department of the Army

The Army describes its requirements in Army Regulation 40-7, "Use of US Food and Drug Administration (FDA) Regulated Investigational Products in Humans Including Schedule 1 Controlled Substances. http://www.apd.army.mil/pdffiles/r40_7.pdf

• Department of Navy (DON)

All research involving the use of investigational test articles (drugs, devices and biologics) shall comply with U.S. Food and Drug Administration (FDA) regulations, references (i) through (m). An Investigational New Drug (IND) application or an Investigational Device Exemption (IDE) must be filed with the FDA whenever research involving human subjects is conducted outside the United States with drugs, devices or biologics, which would require filing of an IND or an IDE if the research were conducted in the United States. Only the Navy SG, Commanders, and Commanding Officers may be designated as sponsors for INDs and IDEs. The Navy SG may consider an IND/IDE equivalency in circumstances where the requirements may not be possible or feasible in international research. Investigators may not be designated as sponsors for INDs and IDEs. [SECNAVINST 3900.39E]

13. PRISONERS OF WAR (POW), OTHER PRISONERS, AND DETAINEES

Research involving human subjects that includes prisoners or human subjects that become prisoners must meet the relevant protections of subpart C of 45CFR46 (DoDI 3216.02). The Georgia Tech IRB will promptly report all decisions involving prisoners as human subjects in research to the HRPO. In addition to the four categories of allowable research with prisoners, two additional conditions are allowable:

1. Epidemiological research that meets the following criteria can also be approved in accordance with the requirements of

subpart C of Reference (h) and the requirements of this Instruction:

1. The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor associations for a disease.

2. The research presents no more than minimal risk.

3. The research presents no more than an inconvenience to the human subject.

4. Prisoners are not a particular focus of the research.

2. Research involving human subjects that would meet the criteria described at section 219.101(b) of Reference (c) can be conducted, but must be approved by a convened IRB and meet the requirements of subpart C of Reference (h), this Instruction, and other applicable requirements. [DoDI 3216.02]

• **Department of the Army**
Research with Prisoners of War (POWs) is prohibited. [AR 70-25]

14. ALLEGATIONS OF NON-COMPLIANCE WITH HUMAN RESEARCH PROTECTIONS

Allegations of non-compliance with DoDI 3216.02 will be properly investigated and reported to the DoD Component supporting the research. All findings of serious or continuing noncompliance with this Instruction that have been substantiated by inquiry or investigation shall be reported to the Assistant Secretary of Defense for Research and Engineering (ASD(R&E)) in a timely manner. [DoDI 3216.02]

• **Department of the Air Force, Department of the Army, and Department of the Navy**
All three departments require the convened IRB to review any serious and continuing non-compliance. The decision of the IRB and notification of the actions taken to remedy the non-compliance is then required to be reported to the IRB Committee, the Institutional Official, and the HRPO for the DoD Component involved in the research. [AFLRI 40-402; AR 70-25; SECNAVINST 3900.39E]

15. CONFLICTING AND COMPETING INTERESTS

Conflicts of interest, not limited to financial conflicts, must be identified and managed appropriately. [DoDI 3216.02; AFRLI 40-402; AR 70-25; SECNAVINST 3900.39E]

16. DOCUMENTATION AND OVERSIGHT THROUGH HEADQUARTERS-LEVEL REVIEW OF RESEARCH PROTOCOLS

A headquarters level or second level review is an additional requirement of the DoD that differs significantly from the NIH review process with which many awardees are familiar. Once a DoD supported study is either determined to be not human subjects research, exempt research involving human subjects, or reviewed and approved as non-exempt research, the study must undergo a HQ level or second level review that is coordinated by the human research oversight office of the DoD component (e.g., Army, Navy, Air Force, etc). Each DoD component has a unique process for accomplishing this required HQ level review. [DoDI 3216.02]

- **Department of the Air Force**

Protocols determined to involve minimal risk may begin once written approval from the GT IRB has been issued. The protocol and records of the approval will then be forwarded to AFMSA/SGE-C for their review and records, but may be subject to modifications or requests for additional information before research can begin.

Protocols determined to involve greater-than-minimal risk, non-lethal weapons, and international research requires approval by AFMSA/SGE-C before research can begin. [AFI 40-402]

- **Department of the Army**

The U.S. Army Medical Research and Materiel Command (USAMRMC) Headquarters' Office of Research Protections oversees the HQ second level review process for USAMRMC supported research. All USAMRMC supported research must be reviewed and approved by the HRPO prior to implementation. Certain research protocols may also be reviewed and approved by the Headquarters, USAMRMC Research Ethics Advisory Panel (REAP). The assigned HSPS will provide additional information for those projects that must be reviewed by the HQ USAMRMC REAP.

Department of Navy (DON)

Protocols determined to involve minimal risk may begin once written approval from the GT IRB has been issued. The protocol and records of the approval will then be forwarded to the DON Human Research

Protection Officials (HRPO) for their review and records, but may be subject to modifications or requests for additional information before research can begin.

Protocols determined to involve greater-than-minimal risk and international research requires approval by the DON HRPO before research can begin. [SECNAVINST 3900.39E]

17. AUDITS, INVESTIGATIONS OR INSPECTIONS OF DEPARTMENT OF NAVY-SUPPORTED RESEARCH

The DON must be notified of any audits, investigations or inspections of DON-supported research. Report the following to the DON Human Research Protections Program (HRPP) Office and appropriate sponsor(s): All suspensions or terminations of previously approved DON supported research protocols; the initiation and results of investigations of alleged noncompliance with human subject protections ; unanticipated problems involving risks to subjects or others, or serious adverse events in DON-supported research; all audits, investigations, or inspections of DON -supported research protocols; all audits, investigations, or inspections of the institution's HRPP conducted by outside entities (e.g., the FDA or OHRP); significant communication between institutions conducting research and other federal departments and agencies regarding compliance and oversight; all restrictions, suspensions, or terminations of institutions' assurances. Report the initiation of all investigations and report results, regardless of the findings, to the Navy Secretary General and appropriate sponsors. [SECNAVINST 3900.E]

18. PUBLICATIONS, PRESENTATIONS OR REPORTS BASED ON THE RESEARCH PROTOCOL

The PI should continue to submit publications, presentations or reports based on the research protocol after closure of the study

- **Department of Air Force**

  Additionally, the Department of the Air Force requires that the IRB receive and maintain copies of publications, presentations or reports based on the research protocol. [AFRLI 40-402]

19. STUDY CLOSURE:

A study closure submission should be submitted to the IRB once all enrollment has ceased and all of the data has been completely de-identified.

- **Department of Air Force**

  Additionally, the Department of the Air Force states that "a study cannot be closed by the IRB administrative office without a report from the PI

confirming that research is complete and there is no further interaction with human subjects or PII data." [AFRLI 40-402]

20. RECORD RETENTION:

The Department of Defense, Component of the Department of Defense, and other auditing agencies may require access to or submission of study records. These records include, but are not limited to: IRB meeting minutes, IRB reviews, IRB decisions, audit reports, study protocol, informed consent, copies of signed informed consent, data, and any other documents used during the study. DoD regulations require that all records are to be retained for a minimum of 3 years after the completion of the research. Other Federal regulations and local policies regarding records must also be followed, as appropriate.

21. PRINCIPAL INVESTIGATOR ACTIONS:

When a research protocol is subject to the DOD Addendum, the IRB letter of approval will contain additional guidance for the Principal Investigator, as follows:

IMPORTANT NOTICE

This study is subject to the Department of Defense (DOD) Addendum to the Georgia Tech Federalwide Assurance (FWA) of Compliance for the Protection of Human Subjects
and therefore must be in compliance with DOD-specific requirements and stipulations.
In particular, please note:

DOD COMPLIANCE CONCURRENCE MUST BE OBTAINED BEFORE WORK WITH HUMAN SUBJECTS MAY BEGIN, DESPITE GEORGIA TECH IRB APPROVAL BEING ISSUED.

DOD compliance concurrence is not another IRB review; rather, it is a process by which the DOD Human Research Protection Official (HRPO) ensures compliance with all applicable regulations and ascertains whether to concur with the civilian IRB's determination.

Obtaining DOD compliance concurrence is the responsibility of the Principal Investigator.
DOD compliance concurrence must be documented in the Georgia Tech IRB record.
Within 60 days of the date of this letter,
please upload the DOD notice of compliance concurrence
and any relevant DOD correspondence to the protocol in IRBWISE.
This must be done prior to starting work with human subjects.

Some of the military components impose additional and varying agency-specific requirements before authorizing work with human subjects to begin. During review of your study, the Georgia Tech IRB contemplated the additional requirements of which we are aware, and those were communicated to you during the review process.

Appendix 16: Scientific Review Template for DOD Protocols

Georgia Institute of Technology Scientific Review Template for conducting independent scientific review of human subjects protocols involving the Department of Defense			
The Department of Defense requires protocols to be scientifically sound prior to review by the institutional review board (IRB); therefore, investigators must address the requirements of the scientific review before proposals are forwarded to the IRB for consideration of human subject protection issues.			
Principal Investigator:		Date of Review:	
Title of Research Protocol:			
SCIENTIFIC REVIEW			
☐ Yes ☐ No	Is the entire proposal well written, logical, and clear? Comments:		
☐ Yes ☐ No	Is the research question articulated with clarity and precision? Comments:		
☐ Yes ☐ No	Is the research question relevant to Army or Navy Medicine? Comments:		
☐ Yes ☐ No	Does the background section inform us why this question is important? Comments:		
☐ Yes ☐ No	Is the literature search comprehensive and complete? Comments:		
☐ Yes ☐ No	Is the proposed design appropriate for the research question being asked? Comments:		
☐ Yes ☐ No	Are the controls adequate? Comments:		
☐ Yes ☐ No	Is it likely that this design will produce a credible answer to the research question? Comments:		
FEASIBILITY			
☐ Yes ☐ No	Are the research methods feasible? Comments:	☐ Yes ☐ No	In the time frame proposed? Comments:

☐ Yes ☐ No	By the personnel who will carry out the study? Comments:	☐ Yes ☐ No	With the resources that are available or requested? Comments:
SAMPLE SIZE			
☐ Yes ☐ No	Are the sample size calculations presented (if needed)? Comments:	☐ Yes ☐ No	Are they credible? Comments:
☐ Yes ☐ No	Is the proposed statistical analysis valid? Comments:		
RECOMMENDATION			
☐ Yes ☐ No	Is the proposal endorsed for its science?		
☐ Yes ☐ No ☐ With changes	Do you recommend this proposal for referral to the Institutional Review Board for consideration of human subject protection issues? If NO or WITH CHANGES, please elaborate:		
Reviewer's Name PRINTED		Reviewer's Signature:	
This completed form should be uploaded to the protocol as a Supplemental Document in IRBWISE.			

Appendix 17: Investigator Agreement

Principal Investigators who propose to conduct a clinical study involving a medical device must complete an Investigator Agreement and include it with their protocol for IRB review.

GEORGIA INSTITUTE OF TECHNOLOGY
INSTITUTIONAL REVIEW BOARD

INVESTIGATOR AGREEMENT
FOR A CLINICAL INVESTIGATION OF THE

_____
(Specify Investigational Device)

_____
(Protocol Number and Study Title)

Relevant Definitions:

- **Clinical investigation** means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.
- **Investigation** is a clinical investigation or research involving one or more subjects to determine the safety and/or effectiveness of a device.
- **Investigator** is an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the investigational device is administered, dispensed to, or used involving a subject. In the event of an investigation being conducted by a team of individuals, "investigator" refers to the responsible leader of that team.
- **Sponsor-investigator** is an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the investigational device is administered, dispensed, or used. The term does not, for example, include a corporation or agency. The obligations of a sponsor-investigator include those of an investigator *and* those of a sponsor.
- **Subject** is a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or who participates as a control. A subject may be in normal health or may have a medical condition or disease.

I AGREE AND/OR CERTIFY THAT:

1. I agree to participate as the Principal Investigator in *a clinical investigation of the investigational device specified above.* I have been provided links to the following Food and Drug Administration (FDA) regulations: 21 CFR Part 812, Investigational Device Exemptions; 21 CFR Part 50, Protection of Human Subjects; and 21 CFR Part 54, Financial Disclosure by Clinical Investigators.

2. I will conduct the clinical investigation in accordance with this agreement; with all requirements of the investigational plan (protocol), Investigational Device Exemption (IDE) regulations, other applicable regulations of the FDA; with adherence to the principles of good clinical practices; and any conditions of approval imposed by the

Georgia Institute of Technology Institutional Review Board (IRB), by any other IRB or Ethics Committee that reviews and approves this study, or by the FDA. I agree to abide by all of the investigator responsibilities enumerated at 21 CFR Part 812, Subpart E and Subpart G, including but not limited to the following:

a. I will obtain written approval from the Georgia Institute of Technology Institutional Review Board in advance of undertaking any activities with human subjects. If I am not also the sponsor-investigator of the corresponding IDE application, I will submit the certification of IRB approval and any conditions of this approval to the sponsor (sponsor-investigator).

c. I will supervise all testing of the *investigational device specified above* on human subjects and will allow only those individuals who are qualified by education, licensure, and/or the governance of the local medical board to perform these tests.

d. I will ensure that Informed Consent is obtained from each subject participating in this clinical investigation in accordance with the informed consent regulation found in 21 CFR Part 50, and that a signed copy of the informed consent shall be available to the sponsor (sponsor-investigator) and the sponsor's (sponsor-investigator's) designated monitor.

e. I will be responsible for accountability of the *investigational device specified above* at the study site and, if I am not also the sponsor-investigator of the corresponding IDE application, I will return all unused *investigational devices specified above* to the sponsor (sponsor-investigator) or otherwise follow the instructions of the sponsor (sponsor-investigator) for disposal of the unused devices.

f. I will ensure the accurate completion of protocol case report forms and, if I am not also the sponsor-investigator of the corresponding IDE application, I will submit completed protocol case report forms, progress reports, and a final report to the sponsor (sponsor-investigator) at the time frames specified in the Protocol and/or FDA regulations.

g. I will direct the retention of required records and documents related to the investigation.

3. I have the appropriate, relevant qualifications to conduct and to oversee the conduct of the investigation as documented by the following: (*Check applicable statement)*

____ My relevant qualifications, including dates, location, extent, and type of experience, are listed in my most recent curriculum vitae (CV), which is attached to this Agreement and which will be maintained by the sponsor (sponsor-investigator) of the corresponding IDE application.

____ My curriculum vitae (CV) does not reflect my relevant qualifications, therefore attached to this Agreement is a statement of my relevant experience (including dates, location(s), extent, and type of experience) which will be maintained by the sponsor (sponsor-investigator) of the corresponding IDE application.

4. There are no reasons to question my ability to oversee the appropriate conduct of this clinical investigation. (Check applicable statement.)

____ I have never participated in an investigation or other research activity which was terminated (disqualified) by FDA, the IRB (or equivalent), or sponsor of a study due to a non-compliance issue.

____ I have participated in an investigation or other research activity which was terminated (disqualified) by FDA, the IRB (or equivalent), or sponsor of a study due to a non-compliance issue. The specific circumstances leading to

this termination and my role in the respective problems or issues and the resolution of these problems or issues are summarized in an attachment to this Agreement.

I further certify that I have not been debarred under the Generic Drug Enforcement Act of 1992, 21 USC §§ 335a and 335b. In the event that I become debarred or receive notice of an action or threat of an action with respect to my debarment during the term of this Agreement, I agree to immediately notify the sponsor (sponsor-investigator) and the Georgia Tech IRB. If I am the sponsor-investigator of the corresponding IDE application, I will also notify the FDA, should I become debarred or receive such notice.

5. Listed below are the names and addresses of all facilities where the study will be conducted, if other than my Georgia Institute of Technology laboratory:

_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____

6. Listed below are the names and addresses of all clinical laboratories, if any, to be used in the study:

_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____

7. Listed below are the names and addresses of all Institutional Review Boards or Ethics Committees, other than the Georgia Institute of Technology IRB, responsible for review of this study. (If this is a multi-site clinical trial, I have listed only those IRBs or Committees that will review my proposed work).

_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____

8. As required by 21 CFR Part 54, Financial Disclosure by Clinical Investigators, I will disclose sufficient and accurate financial information to the sponsor (sponsor-investigator) and to the Georgia Tech Institutional Review Board by completing the Certification of Financial Interest form (attached). If applicable, I will also submit to the Georgia Tech IRB the determination letter and/or management plan from the Georgia Tech Research Corporation (GTRC) Office of Conflict of Interest Management. I will also notify the sponsor (sponsor-investigator) and the Georgia Tech IRB if my disclosed financial information changes at any time during the investigation or up to one year following the closure of the study.

PRINCIPAL INVESTIGATOR:

_____

Name of Principal Investigator (please print or type)

_____ _____

Signature of Principal Investigator Date

CO-PRINCIPAL INVESTIGATORS AND INVESTIGATORS : A current CV or statement of relevant experience and a completed Certification of Financial Interest form and, if applicable, letter of determination and copy of your COI management plan is required to be submitted to the sponsor (sponsor-investigator) for each Co-Principal Investigator or Investigator listed below.

As a Co-Principal Investigator or Investigator for this investigation, I have read the foregoing and agree to be bound by its terms.

_____

Name (please print or type)

_____ _____

Signature Date

_____

Name (please print or type)

_____ _____

Signature Date

_____

Name (please print or type)

_____ _____

Signature Date

Certification of Financial Interest of Investigators

Title of Study: _____

_____

Principal Investigator: _____

Name of Investigational Drug/Device: _____

As an investigator who will be participating in the above-specified clinical study being conducted under a University-based (i.e., investigator-sponsored) or University-sponsored IND or IDE application, I certify that *(check the appropriate box for each statement):*

[ ] I do [ ] I do not Have an ownership interest, stock options, or other financial interest (i.e., *equity interest*) in the company (public or non-public) that owns the investigational drug or device being evaluated in the clinical study.

[ ] I do [ ] do not Have property or other financial interest (i.e., *proprietary interest*) in the investigational drug or device being evaluated in this clinical study;

including, but not limited to, a patent or patent interest, trademark, copyright, licensing agreement, or any arrangement tied to a current or future right to receive royalties associated with the development or eventual commercialization of the drug or device.

[ ] I will [ ] I will not Receive payments from the company (i.e., other than the University) that owns the respective investigational drug or device during the term of the conduct of the clinical study; nor do I anticipate receiving payments from the company during a 1 year period following completion of the study. Applicable payments (i.e., *financial interest*) include, but are not limited to, grants to fund projects or research or compensation in the form of monetary payments, equipment, or retainers for consultation or honoraria.

If the response to any of the above statements is affirmative, submission of your approved Conflict of Interest Management Plan is required.

_____

Name of Investigator (Printed or Typed)

_____ _____

Signature of Investigator Date

Guidance for Industry
Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology

Contains Nonbinding Recommendations

June, 2014

Additional copies are available from:
Office of Policy
Office of the Commissioner
Food and Drug Administration
10903 New Hampshire
Avenue Silver Spring, MD
20993 Phone: 301-796-
4830
http://www.fda.gov/RegulatoryInformation/Guidances/ucm257698.htm

You may submit electronic or written comments regarding this guidance at any time. Submit written comments on the guidance to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.regulations.gov. All comments should be identified with the docket number (FDA-2010-D-0530) listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document contact: Office of the Commissioner, Food and Drug Administration, 10903 New Hampshire Avenue, Silver Spring, MD 20993, 301-796-4830.

U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner

June 2014

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Guidance for Industry
Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology[1]

This guidance represents the Food and Drug Administration's (FDA's or the Agency's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the telephone number listed on the title page of this guidance.

I. INTRODUCTION AND SCOPE

Nanotechnology is an emerging technology that can be used in a broad array of FDA-regulated products, including medical products (*e.g*. to increase bioavailability of a drug), foods (*e.g*., to improve food packaging) and cosmetics (*e.g*. to affect the look and feel of cosmetics). Materials in the nanoscale range (i.e., with at least one dimension in the size range of approximately 1 nanometer (nm) to 100 nm) can exhibit different chemical or physical properties, or biological effects compared to larger-scale counterparts. For example, dimension-dependent properties or phenomena may be used for functional effects such as increased bioavailability, decreased dosage, or increased potency of a drug product, decreased toxicity of a drug product, better detection of pathogens, more protective food packaging materials, or improved delivery of a functional ingredient or a nutrient in food (Refs. 1-6). These effects may derive from altered chemical, biological, or magnetic properties, altered electrical or optical activity, increased structural integrity, or other unique characteristics of materials in the nanoscale range not normally observed or expected in larger-scale materials with the same chemical composition (Ref. 7). Materials or end products may also exhibit similar properties or phenomena attributable to a dimension(s) outside the

[1] This guidance finalizes the draft guidance, entitled "Draft Guidance for Industry: Considering Whether an FDARegulated Product Involves the Application of Nanotechnology," which was issued in June, 2011. This guidance was prepared by FDA's Office of Policy in the Office of the Commissioner, in consultation with FDA's Center for Biologics Evaluation and Research, Center for Drugs Evaluation and Research, Center for Devices and Radiological Health, Center for Food Safety and Applied Nutrition, Center for Tobacco Products, Center for Veterinary
Medicine, National Center for Toxicological Research, Office of the Chief Scientist, Office of Foods and Veterinary Medicine, Office of Regulatory Affairs, Office of Special Medical Programs, and Nanotechnology Task Force.

nanoscale range of approximately 1 nm to 100 nm (Refs. 27-30; see also discussion in Section II.B.5).

For the purpose of this guidance only, references to "products that involve the application of nanotechnology" or "nanotechnology products" mean products that contain or are manufactured using materials in the nanoscale range, as well as products that contain or are manufactured using certain materials that otherwise exhibit related dimension-dependent properties or phenomena. Likewise, we use the term "nanomaterial" generally to refer to both materials in the nanoscale range and certain materials that otherwise exhibit related dimension-dependent properties or phenomena. Use of these terms is for the purpose of communicating FDA's current thinking elaborated in this document only.

As used in this guidance, the word "products" (or "FDA-regulated products") is meant to include products, materials, ingredients, and other substances regulated by FDA, including drugs, biological products, medical devices, food substances (including food for animals), dietary supplements, cosmetic products, and tobacco products.[2]

The guidance describes FDA's current thinking on determining whether FDA-regulated products involve the application of nanotechnology. This guidance is intended for manufacturers, suppliers, importers, and other stakeholders. (For convenience, the guidance will refer to these parties as "industry.") FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidance documents describe FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance documents means that something is suggested or recommended, but not required.

The application of nanotechnology may result in product attributes that differ from those of conventionally-manufactured products, and thus may merit particular examination. However, FDA (or "we") does not categorically judge all products that involve the application of nanotechnology as intrinsically benign or harmful. FDA will regulate nanotechnology products under existing statutory authorities, in accordance with the specific legal standards applicable to each type of product under its jurisdiction. We consider the current framework for safety assessment sufficiently robust and flexible to be appropriate for a variety of materials, including nanomaterials. FDA maintains a product-focused, science-based regulatory policy. Technical assessments will be product-specific, taking into account the effects of nanomaterials in the particular biological and mechanical context of each product and its intended

[2] Nanotechnology may also be applied to combination products (as defined at 21 CFR 3.2(e)).

use. As such, the particular policies for each product area, both substantive and procedural, will vary according to the statutory authorities and relevant regulatory frameworks (Ref. 8). We believe that this regulatory policy allows for tailored approaches that adhere to applicable legal frameworks and reflect the characteristics of specific products or product classes and evolving technology and scientific understanding.

This guidance provides an overarching framework for FDA's approach to the regulation of nanotechnology products. It identifies two points to consider when determining whether the FDA-regulated product involves the application of nanotechnology. An affirmative finding to either of the Points to Consider, elaborated in section II below, might suggest the need for particular attention by the Agency and/or industry to the product to identify and address potential implications for safety, effectiveness, public health impact, or regulatory status of the product.

This guidance does not address, or presuppose, what ultimate regulatory outcome, if any, will result in a particular case where the use of these points may indicate that an FDA-regulated product involves the application of nanotechnology. Issues such as the safety, effectiveness, public health impact, or the regulatory status of nanotechnology products are currently addressed on a case-by-case basis using FDA's existing review processes.[3]

This guidance also does not establish regulatory definitions. Rather, it is intended to help industry and others identify when they should consider potential implications for regulatory status, safety, effectiveness, or public health impact that may arise with the application of nanotechnology in FDA-regulated products. We advise industry to consult with FDA early in the development process to facilitate a mutual understanding of the specific scientific and regulatory issues for their nanotechnology products.

FDA will provide further guidance to industry, as needed, to address the application of nanotechnology as applicable to specific FDA-regulated products or classes of products (such as human foods, drugs, or cosmetics), consistent with existing federal policies (Refs. 9, 10). As appropriate, FDA's product-specific guidance documents will address issues such as the regulatory status, safety, effectiveness, performance, quality, or public health impact of nanotechnology products.[4]

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[3] It bears noting that the application of nanotechnology may also affect the classification of a product. For example, nanomaterials used in medical products may function through different modes of action than larger-scale materials with the same chemical composition, which may affect the classification of the product, for example as a drug or device.

[4] FDA's guidance documents relevant to nanotechnology, including product-specific guidance documents that focus on nanotechnology applications in specific product sectors, can be found at:

II. DISCUSSION

FDA has not established regulatory definitions of "nanotechnology," "nanomaterial," "nanoscale," or other related terms. These terms are commonly used in relation to the engineering (i.e., deliberate manipulation, manufacture or selection) of materials that have at least one dimension in the size range of approximately 1 nanometers (nm) to 100 nm. For example, the National Nanotechnology Initiative Program defines nanotechnology as "the understanding and control of matter at dimensions between approximately 1 and 100 nanometers, where unique phenomena enable novel applications" (Ref. 11). Various published definitions mention other factors such as function, shape, charge, the ratio of surface area to volume, or other physical or chemical properties.

Based on our current scientific and technical understanding of nanomaterials and their characteristics, FDA believes that evaluations of safety, effectiveness, public health impact, or regulatory status of nanotechnology products should consider any unique properties and behaviors that the application of nanotechnology may impart. This guidance identifies two Points to Consider that should be used to evaluate whether FDA-regulated products involve the application of nanotechnology. These points address both particle dimensions and dimensiondependent properties or phenomena. Product-specific premarket review, when required, offers an opportunity for FDA to apply these points and, where products are not subject to premarket review, industry should consider these points. If either point applies to a given product, industry and FDA should consider whether the evaluations of safety, effectiveness, public health impact, or regulatory status of that product have identified and adequately addressed any unique properties or behaviors of the product.

These two Points to Consider are intended to provide an initial screening tool that can be broadly applied to all FDA-regulated products, with the understanding that these points are subject to change in the future as new information becomes available. In particular, FDA may further refine these points, either as applicable broadly to all FDA-regulated products or as applicable to particular products or classes of products, as justified by scientific information. This may include refining particle size parameters or introducing additional parameters such as those related to particle size distribution or specific properties.[5] We will consider future revisions to our

http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/default.htm

[5] At this time, we do not have an adequate basis on which to determine a particle number threshold or a list of "unique" or "novel" properties that are applicable across the range of FDA-regulated products. In addition,

approach, including developing regulatory definitions relevant to nanotechnology, as warranted and in keeping with evolving scientific understanding. As previously indicated, FDA also may provide additional guidance, including product-specific guidance documents, to address issues such as the regulatory status, safety, effectiveness, performance, quality, or public health impact of nanotechnology products.

A. Points to Consider

At this time, when considering whether an FDA-regulated product involves the application of nanotechnology, FDA will ask:

1. Whether a material or end product is engineered to have at least one external dimension, or an internal or surface structure, in the nanoscale range (approximately 1 nm to 100 nm);

In addition, as we explain in more detail below, because materials or end products can also exhibit related properties or phenomena attributable to a dimension(s) outside the nanoscale range of approximately 1 nm to 100 nm that are relevant to evaluations of safety, effectiveness, performance, quality, public health impact, or regulatory status of products, we will also ask:

2. Whether a material or end product is engineered to exhibit properties or phenomena, including physical or chemical properties or biological effects, that are attributable to its dimension(s), even if these dimensions fall outside the nanoscale range, up to one micrometer (1,000 nm).[6]

These considerations apply not only to new products, but also when changes to manufacturing processes alter the dimensions, properties, or effects of an FDA-regulated product or any of its constituent parts.[7]

B. Rationale for Elements within the Points to Consider

challenges related to measurement methods and biological effects add further complexity to recommending use of particle number, weight, or surface area as the most appropriate units of measure. FDA intends to actively follow scientific developments on this issue and provide additional guidance, as appropriate.

[6] As explained in section II.B.5. below, the use of 1,000 nm as a reference point should not be interpreted to mean that materials or products with dimensions above 1,000 nm cannot exhibit dimension-dependent properties or phenomena of importance to safety, effectiveness, public health impact, or regulatory status of the material or product. See further discussion on this issue in section II.B.5. below.

[7] These Points to Consider are not intended to apply to products that have been previously reviewed or approved by FDA and where no changes are made to manufacturing processes that would alter the dimensions, properties or effects of the product or its constituent parts.

1. Material or end product that is *engineered* to have certain dimensions or exhibit certain properties (in Points 1 and 2)

The term "engineered," used in both Points 1 and 2, is used to distinguish products that have been deliberately manipulated by the application of nanotechnology from those products that contain materials that naturally occur in the nanoscale range. FDA is particularly interested in the *deliberate* and *purposeful* manipulation and control of dimensions to produce specific properties, because the emergence of these new properties or phenomena may raise questions about the safety, effectiveness, performance, quality or public health impact that may warrant further evaluation. FDA's interest in materials or products "engineered" to have nanoscale dimensions or related dimension-dependent properties or phenomena is distinct from the more familiar use of biological or chemical substances that may naturally exist at small scales, including at the nanoscale, such as microorganisms or proteins.

The term "engineered" is also used to distinguish products that have been deliberately manipulated by the application of nanotechnology from products that may unintentionally include materials in the nanoscale range. For example, the incidental presence of particles in the nanoscale range in conventionallymanufactured products[8] is not covered under the scope of this guidance.[9]

2. Material or end product (in Points 1 and 2)

The phrase "material or end product," referred to in both Points 1 and 2, is used to cover different types of articles that are regulated by FDA, such as products, materials, ingredients, and other substances regulated by FDA. This includes finished products (e.g., a drug tablet for administration to a patient) as well as materials that are intended for use in a finished product (e.g., a food additive added to a food during processing). In determining whether a material or end product satisfies either Point 1 or Point 2, FDA will examine the material or end product, and may also consider the constituent parts of the material or end product. Therefore, relevant considerations include whether a material or end product contains or involves in its manufacture the use of materials that meet either Point 1 or Point 2.

[8] For example, small amounts of particles in the nanoscale range have been reported to be present in foods manufactured using conventional food manufacturing practices (Ref. 12).

[9] However, evaluations of conventionally-manufactured products may include a consideration of the effects, if any, of such incidental presence of particles in the nanoscale range on the safety, effectiveness, or public health impact of a product.

3. At least one external dimension, or an internal or surface structure, in the nanoscale range (approximately 1 nm to 100 nm) (in Point 1)

A size range of approximately 1 nm to 100 nm is commonly used in various working definitions or descriptions regarding nanotechnology proposed by the regulatory and scientific community.[10] In this size range, materials can exhibit new or altered physicochemical properties that can enable novel applications (Refs. 11, 13-15). Accordingly, per Point 1, if a material or end product is engineered to have at least one external dimension in the range of 1 nm to 100 nm, or is engineered to have an internal or surface structure in the range of 1 nm to 100 nm, industry and FDA should consider any unique characteristics or biological effects exhibited by the product that may influence its safety, effectiveness, public health impact, or regulatory status. Primary particles engineered with at least one external dimension within the nanoscale range are covered in Point 1. This Point also covers any aggregates or agglomerates formed by such nanoscale primary particles. In addition, coated, functionalized, or hierarchically-assembled engineered structures that include internal or surface discrete and functional nanoscale entities, such as where such entities are embedded or attached to the surface, are encompassed within Point 1.[11] Such engineered structures with discrete and functional nanoscale entities embedded or attached to the surface may have altered properties or phenomena that may affect product safety or effectiveness (Ref. 16). The inclusion of particles, objects, or structures with internal, surface, or external dimension(s) in the nanoscale range is consistent with approaches taken by other scientific and regulatory bodies (Refs. 17-23).

4. Properties or phenomena attributable to dimension(s) (in Point 2)

While size alone, for very small particles, is suggestive of the presence of properties meriting further examination, the identification and assessment of specific dimension-dependent properties and phenomena are ultimately more relevant for purposes of FDA regulatory review and oversight. Point 2, therefore, focuses on the properties of the material and its behavior in biological systems.[12] The phrase "exhibits properties or phenomena . . . that are attributable to its dimension(s)," is used because properties and phenomena of materials in the nanoscale range enable applications that can affect the safety, effectiveness, performance, quality, public health impact, or regulatory status of FDA-regulated products. For example, as noted above, dimension-dependent properties or phenomena may be used for various functional effects such as increased bioavailability or decreased toxicity of drug products, better detection of pathogens,

[10] For example, a size range of approximately 1 nm to 100 nm is used in definitions, working definitions, or descriptions published by the National Nanotechnology Initiative (Ref. 11); Environmental Protection Agency (http://www.epa.gov/pesticides/regulating/nanotechnology.html); European Commission (Ref. 17); Health Canada (Ref. 19); International Standards Organization (Ref. 20); Organization for Economic Cooperation and Development's Working Party on Nanotechnology and Working Party on Manufactured Nanomaterials (http://www.oecd.org/sti/nano/); National Cancer Institute (http://www.cancer.gov/dictionary?cdrid=445071); and American National Standards Institute (http://nanostandards.ansi.org/tiki-index.php).

[11] This is not intended to include any incidental presence of internal or surface features with dimensions in the nanoscale range that may be present in conventionally-manufactured substances (for example, internal porosity, surface roughness or surface defects).

[12] Consistent with "Policy Principles for the U.S. Decision-Making Concerning Regulation and Oversight of Applications of Nanotechnology and Nanomaterials," Office of Science and Technology Policy, Office of Management and Budget, and Office of the United States Trade Representative, June 9, 2011 (Ref. 10).

improved food packaging materials, or improved delivery of nutrients. These effects may derive from altered or unique characteristics of materials in the nanoscale range that are not normally observed or expected in larger-scale materials with the same chemical composition (Ref. 7). However, such changes may raise questions about the safety, effectiveness, performance, quality or public health impact of nanotechnology products. In addition, considerations such as routes of exposure, dosage, and behavior in various biological systems (including specific tissues and organs) (Refs. 13, 24) are critical for evaluating the safety, effectiveness, public health impact, or regulatory status of a wide array of products under FDA's jurisdiction. Such evaluations should include a consideration of the specific tests (whether traditional, modified, or new) that may be needed (Refs. 25, 26) to determine the physicochemical properties and biological effects of a product that involves the application of nanotechnology.

5. Dimension(s) of up to one micrometer (1,000 nm) (in Point 2)

Materials or end products can also exhibit properties or phenomena attributable to a dimension(s) outside the nanoscale range of approximately 1 nm to 100 nm. Physical and chemical properties and biological behavior that are relevant to evaluations of safety, effectiveness, performance, quality, public health impact, or regulatory status of products have been observed at dimensions outside the nanoscale range of approximately 1 nm to 100 nm (Refs. 27-30). Therefore, Point 2 focuses on the importance of considering properties or phenomena attributable to dimensions, even where such dimensions may be outside the nanoscale range of approximately 1 nm to 100 nm. FDA's consideration of materials with dimension(s) outside the nanoscale

range of approximately 1 nm to 100 nm is consistent with approaches taken by other scientific and regulatory organizations.[10]

At the present time, available scientific information does not establish a uniform upper boundary above 100 nm where novel properties and phenomena similar to those seen in materials with dimensions in the nanoscale range cease for all potential materials or end products. For this reason, at this time, FDA finds it reasonable to consider evaluation of materials or end products engineered to exhibit properties or phenomena attributable to dimensions up to 1,000 nm, as a means to screen materials for further examination and to determine whether these materials exhibit properties or phenomena attributable to their dimension(s) and associated with the application of nanotechnology.[14] An upper limit of one micrometer (1,000 nm) applied in the context of properties or phenomena attributable to dimensions serves both to: (1) include materials with dimension(s) outside the nanoscale range of approximately 1 nm to 100 nm that may exhibit dimension-dependent properties or phenomena associated with the application of nanotechnology and distinct from those of macro-scaled materials; and (2) exclude macro-scaled materials that may have properties attributable to their dimension(s) but are not likely associated with the application of nanotechnology.

[10] For example, the Joint Research Centre and the Scientific Committee on Emerging and Newly Identified Health Risks of the European Commission concluded: "In order to base a nanomaterials definition for regulatory purposes on size alone, the upper nanoscale limit should ideally be high enough to capture all types of materials that would need particular attention for regulation due to their nanoscale size. Upper limits which are often used in existing definitions, for example 100 nm, may require the introduction of one or more qualifiers based on structural features or properties other than size, in order to capture structures of concern (for example agglomerates or aggregates) with a size larger than 100 nm in the regulation" (Ref. 22); "The upper size limit for one or more external dimensions of 100 nm is complicated by the potential exclusion of aggregates, agglomerates and multicomponent assemblies that would have external sizes greater than this" (Ref. 23); and "An upper limit of 100 nm is commonly used by general consensus but there is no scientific evidence to support the appropriateness of this value (Stated as SCENIHR conclusions in the European Commission Recommendation on the definition of nanomaterial, Ref. 17). The European Commission further noted that "it may be necessary to include additional materials, such as some materials with a size . . . greater than 100 nm in the scope of application of specific legislation or legislative provisions suited for a nanomaterial (Ref. 17). In addition, the International Organization for Standardization (ISO) "acknowledged that health and safety considerations associated with intentionally produced and incidental nanoobjects do not abruptly end at dimensions of 100 nm. As knowledge expands, it is abundantly clear that a robust terminology will need to capture and convey effectively the performance aspects of intentionally produced nanoobjects and nanostructured materials in their definitions, apart from their fundamental size and shape" (Ref. 20). More recently, Health Canada adopted a working definition of nanomaterial that, in part, reflects that it is possible for nanoscale properties/ phenomena to be exhibited outside the 1 nm to 100 nm size range, such as select quantum devices (Ref. 19). Finally, in its second regulatory review on nanomaterials, the European Commission noted that "fullerenes, graphene flakes and single wall carbon nanotubes with one or more external dimensions below 1 nm should be considered as nanomaterials." Several types of nanomaterials were identified as not matching the EU definition, with an acknowledgment that "there are an increasing number of particles which are engineered to have internal nanoscale features. Examples are core-shell particles and nano-encapsulates. These particles may be designed, for example for pharmaceutical applications, where the inner core particle is "released" in a certain

An upper limit of 1,000 nm, combined with the presence of dimension-dependent properties or phenomena similar to those seen in materials with dimensions in the nanoscale range, provides an initial screening tool to help identify materials or products with properties or phenomena of particular relevance for regulatory review. The use of 1,000 nm as a reference point in this context should not be interpreted to mean that materials or products with dimensions above 1,000 nm cannot exhibit dimension-dependent properties or phenomena of importance to safety, effectiveness, public health impact, or regulatory status of the material or product. As noted above, we may further refine these Points to Consider, including this upper limit, either as applicable broadly to FDA-regulated products or as applicable to specific products or product categories.

III. CONCLUSION

The two Points to Consider elaborated in this guidance should be applied when considering whether an FDA-regulated product involves the application of nanotechnology. An affirmative finding to either of the Points to Consider, elaborated in this guidance, might suggest the need for particular attention to the product by FDA and/or industry for potential implications for safety, effectiveness, public health impact, or regulatory status of the product. We will consider future revisions to our approach, including developing regulatory definitions relevant to nanotechnology, as warranted and in keeping with evolving scientific understanding.

There remains a need to learn more about the potential role and importance of dimensions in the physical and chemical characteristics and biological effects exhibited by FDA-regulated products

environment. Some of these materials have an external diameter smaller than 100 nm, matching the EU nanomaterial definition, others have an external diameter larger than 100 nm, not matching the EU nanomaterial definition" (Ref. 31).

[14] However, as noted previously, FDA will consider further refinement of these Points to Consider for particular products or classes of products, as scientific information becomes available, including refining particle size parameters.

that involve the application of nanotechnology.[11] Product-specific premarket review, when required, offers an opportunity for FDA to better understand the properties and behavior of products that involve the application of nanotechnology. Where products that involve the application of

[11] FDA's nanotechnology regulatory science program aims to further enhance FDA's scientific capabilities, including developing necessary data and tools to identify and measure dimension-dependent properties and assess their potential impact on safety or effectiveness. *See* http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/ucm273325.htm

nanotechnology are not subject to premarket review, we urge industry to consult with the Agency early in the product development process. In this way, any questions about the products' regulatory status, safety, effectiveness, or public health impact can be appropriately and adequately addressed. FDA has and, as needed, will continue to provide additional guidance to industry in more targeted guidance documents to address these considerations.

IV. REFERENCES

We have placed these references on display in the Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. You may see them at that location between 9 a.m. and 4 p.m., Monday through Friday. As of June 1, 2014, FDA had verified the Web site addresses for the references it makes available as hyperlinks from the Internet copy of this guidance, but FDA is not responsible for any subsequent changes to Non- FDA Web site references after June 1, 2014.

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Appendix 19: FDA Guidance for Sponsors, Clinical Investigators, and IRBs Regarding FDA Form 1572

Guidance for Industry

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

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

Procedural
October 2009

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

Additional copies are available from:
Office of Training and Communication
Division of Drug Information, HFD-240
Center for Drug Evaluation and Research
Food and Drug Administration
(Tel) 301-827-4573
http://www.fda.gov/cder/guidance/index.htm
or
Office of Communication, Training and
Manufacturers Assistance, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
http://www.fda.gov/cber/guidelines.htm
(Tel) 800-835-4709 or 301-827-1800
or
Office of Health and Industry Programs
Division of Small Manufacturers, International, and Consumer Assistance, HFZ-220
Center for Devices and Radiological Health
Food and Drug Administration
Tel: 1-800-638-2041
www.fda.gov/cdrh

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

Procedural

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Contains Nonbinding Recommendations

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Guidance for Industry [12]
Investigator Responsibilities—Protecting the Rights, Safety, and Welfare of Study Subjects

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This guidance provides an overview of the responsibilities of a person who conducts a clinical investigation of a drug, biological product, or medical device (an *investigator* as defined in 21 CFR 312.3(b) and 21 CFR 812.3(i)). The goal of this guidance is to help investigators better meet their responsibilities with respect to protecting human subjects and ensuring the integrity of the data from clinical investigations. This guidance is intended to clarify for investigators and sponsors FDA's expectations concerning the investigator's responsibility (1) to supervise a clinical study in which some study tasks are delegated to employees or colleagues of the investigator or other third parties and (2) to protect the rights, safety, and welfare of study subjects.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. OVERVIEW OF INVESTIGATOR RESPONSIBILITIES

In conducting clinical investigations of drugs, including biological products, under 21 CFR part 312 and of medical devices under 21 CFR part 812, the investigator is responsible for:

- Ensuring that a clinical investigation is conducted according to the signed investigator statement for clinical investigations of drugs, including biological products, or agreement for clinical investigations of medical devices, 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)

[12] This guidance has been prepared by the Investigator Responsibilities Working Group, which includes representatives from the Office of the Commissioner, the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and the Center for Devices and Radiological Health (CDRH) at the Food and Drug Administration.

Although specific investigator responsibilities in drug and biologics clinical trials are not identical to the investigator responsibilities in medical device clinical trials, the general responsibilities are essentially the same. This guidance discusses the general investigator responsibilities that are applicable to clinical trials of drugs, biologics, and medical devices.

An investigator's responsibilities in conducting clinical investigations of ***drugs*** or ***biologics*** are provided in 21 CFR Part 312. Many of these responsibilities are included in the required investigator's signed statement, Form FDA-1572 (see Attachment A) (hereinafter referred to as 1572). Note that although the 1572 specifically incorporates most of the requirements directed at investigators in part 312, not all requirements are listed in the 1572. Investigators and sponsors should refer to 21 CFR Parts 11, 50, 54, 56, and 312 for a more comprehensive listing of FDA's requirements for the conduct of drug and biologics studies. [13]

An investigator's responsibilities in conducting clinical investigations of a ***medical device*** are provided in 21 CFR Part 812, including the requirement that there be a signed agreement between the investigator and sponsor (see 21 CFR 812.43(c)(4) and 812.100). The medical device regulations do not require use of a specific form for an investigator's statement; and there are additional requirements not listed above (see Attachment B). Investigators and sponsors should refer to 21 CFR Parts 11, 50, 54, 56, and 812 for a more comprehensive listing of FDA's requirements for the conduct of device studies.

Nothing in this guidance is intended to conflict with recommendations for investigators contained in the International Conference on Harmonisation (ICH) guidance for industry, *E6 Good Clinical Practice: Consolidated Guidance* (Good Clinical Practice Guidance).[14]

III. CLARIFICATION OF CERTAIN INVESTIGATOR RESPONSIBILITIES

This section of the guidance clarifies the investigator's responsibility to supervise the conduct of the clinical investigation and to protect the rights, safety, and welfare of participants in drug and medical device clinical trials.

A. Supervision of the Conduct of a Clinical Investigation

As stated above, investigators who conduct clinical investigations of drugs, including biological products, under 21 CFR Part 312, commit themselves to personally conduct or supervise the investigation. Investigators who conduct clinical investigations of medical devices, under 21 CFR Part 812, commit themselves to supervise all testing of the device involving human subjects. 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

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[13] As a reminder, some investigators may be responsible for submitting certain clinical trial information to the National Institutes of Health clinical trials data bank under 42 U.S.C 282(j), 402(j) of the Public Health Service Act. Although not all investigators will be expected to meet this requirement, go to www.clinicaltrials.gov, for further information about potential responsibilities.

[14] Guidances, including ICH guidances, are available on the Agency's Web page. See the Web addresses on the second title page of this guidance.

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.
In assessing the adequacy of supervision by an investigator, FDA focuses on four major areas: (1) whether individuals who were delegated tasks were qualified to perform such tasks, (2) whether study staff received adequate training on how to conduct the delegated tasks and were provided with an adequate understanding of the study, (3) whether there was adequate supervision and involvement in the ongoing conduct of the study, and (4) whether there was adequate supervision or oversight of any third parties involved in the conduct of a study to the extent such supervision or oversight was reasonably possible.

1. What Is Appropriate Delegation of Study-Related Tasks?

The investigator should ensure that any individual to whom a task is delegated is qualified by education, training, and experience (and state licensure where relevant) to perform the delegated task. Appropriate delegation is primarily an issue for tasks considered to be clinical or medical in nature, such as evaluating study subjects to assess clinical response to an investigational therapy (e.g., global assessment scales, vital signs) or providing medical care to subjects during the course of the study. Most clinical/medical tasks require formal medical training and may also have licensing or certification requirements. Licensing requirements may vary by jurisdiction (e.g., states, countries). Investigators should take such qualifications/licensing requirements into account when considering delegation of specific tasks. In all cases, a qualified physician (or dentist) should be responsible for all trial-related medical (or dental) decisions and care.[15]

During inspections of investigation sites, FDA has identified instances in which study tasks have been delegated to individuals lacking appropriate qualifications. Examples of tasks that have been inappropriately delegated include:

- Screening evaluations, including obtaining medical histories and assessment of inclusion/exclusion criteria
- Physical examinations
- Evaluation of adverse events
- Assessments of primary study endpoints
- Obtaining informed consent

The investigator is responsible for conducting studies in accordance with the protocol (see 21 CFR 312.60, Form FDA-1572, 21 CFR 812.43 and 812.100). In some cases a protocol may specify the qualifications of the individuals who are to perform certain protocol-required tasks (e.g., physician, registered nurse), in which case the protocol must be followed even if state law permits individuals with different qualifications to perform the task (see 21 CFR 312.23(a)(6) and 312.40(a)(1)). For example, if the state in which the study site is located permits a nurse practitioner or physician's assistant to perform physical examinations under the supervision of a physician, but the protocol specifies that physical examinations must be done by a physician, a physician must perform such exams.

[15] Guidance for industry, *E6 Good Clinical Practice: Consolidated Guidance*, section 4.3.1.

The investigator should maintain a list of the appropriately qualified persons to whom significant trial-related duties have been delegated.[16] This list should also describe the delegated tasks, identify the training that individuals have received that qualifies them to perform delegated tasks (e.g., can refer to an individual's CV on file), and identify the dates of involvement in the study. An investigator should maintain separate lists for each study conducted by the investigator.

2. What Is Adequate Training?

The investigator should ensure that there is adequate training for all staff participating in the conduct of the study, including any new staff hired after the study has begun to meet unanticipated workload or to replace staff who have left. The investigator should ensure that staff:

- Are familiar with the purpose of the study and the protocol
- Have an adequate understanding of the specific details of the protocol and attributes of the investigational product needed to perform their assigned tasks
- Are aware of regulatory requirements and acceptable standards for the conduct of clinical trials and the protection of human subjects
- Are competent to perform or have been trained to perform the tasks they are delegated
- Are informed of any pertinent changes during the conduct of the trial and receive additional training as appropriate

If the sponsor provides training for investigators in the conduct of the study, the investigator should ensure that staff receive the sponsor's training, or any information (e.g., training materials) from that training that is pertinent to the staff's role in the study.

3. What Is Adequate Supervision of the Conduct of an Ongoing Clinical Trial?

For each study site, there should be a distinct individual identified as an investigator who has supervisory responsibility for the site. Where there is a subinvestigator at a site, that individual should report directly to the investigator for the site (i.e., the investigator should have clear responsibility for evaluating the subinvestigator's performance and the authority to terminate the subinvestigator's involvement with the study) and the subinvestigator should not be delegated the primary supervisory responsibility for the site.

The investigator should have sufficient time to properly conduct and supervise the clinical trial. The level of supervision should be appropriate to the staff, the nature of the trial, and the subject population. In FDA's experience, the following factors may affect the ability of an investigator to provide adequate supervision of the conduct of an ongoing clinical trial at the investigator's site:

- Inexperienced study staff
- Demanding workload for study staff
- Complex clinical trials (e.g., many observations, large amounts of data collected)
- Large number of subjects enrolled at a site

[16] [5] Ibid, section 4.1.5

- A subject population that is seriously ill
- Conducting multiple studies concurrently
- Conducting a study from a remote (e.g., off-site) location
- Conducting a study at multiple sites under the oversight of a single investigator, particularly where those sites are not in close proximity

The investigator should develop a plan for the supervision and oversight of the clinical trial at the site. Supervision and oversight should be provided even for individuals who are highly qualified and experienced. A plan might include the following elements, to the extent they apply to a particular trial:

- Routine meetings with staff to review trial progress, adverse events, and update staff on any changes to the protocol or other procedures
- Routine meetings with the sponsor's monitors
- A procedure for the timely correction and documentation of problems identified by study personnel, outside monitors or auditors, or other parties involved in the conduct of a study
- A procedure for documenting or reviewing the performance of delegated tasks in a satisfactory and timely manner (e.g., observation of the performance of selected assessments or independent verification by repeating selected assessments)
- A procedure for ensuring that the consent process is being conducted in accordance with 21 CFR Part 50 and that study subjects understand the nature of their participation and the risks
- A procedure for ensuring that source data are accurate, contemporaneous, and original
- A procedure for ensuring that information in source documents is accurately captured on the case report forms (CRFs)
- A procedure for dealing with data queries and discrepancies identified by the study monitor
- Procedures for ensuring study staff comply with the protocol and adverse event assessment and reporting requirements
- A procedure for addressing medical and ethical issues that arise during the course of the study in a timely manner

4. What Are an Investigator's Responsibilities for Oversight of Other Parties Involved in the Conduct of a Clinical Trial?

a. Study Staff Not in the Direct Employ of the Investigator

Staff involved directly in the conduct of a clinical investigation may include individuals who are not in the direct employ of the investigator. For example, a site management organization (SMO) may hire an investigator to conduct a study and provide the investigator with a study coordinator or nursing staff employed by the SMO. In this situation, the investigator should take steps to ensure that the staff not under his/her direct employ are qualified to perform delegated tasks (see section III.A.1) and have received adequate training on carrying out the delegated tasks and on the nature of the study (see section III.A.2), or the investigator should provide such training. The investigator should be particularly cautious where documentation needed to comply with the investigator's regulatory responsibilities is developed and maintained by SMO staff (e.g., source documents, CRFs, drug

storage and accountability records, institutional review board correspondence). A sponsor who retains an SMO shares responsibility for the quality of the work performed by the SMO.

The investigator is responsible for supervising the study tasks performed by this staff, even though they are not in his/her direct employ during the conduct of the study (see section III.A.3). This responsibility exists regardless of the qualifications and experience of staff members. In the event that the staff's performance of study-related tasks is not adequate and cannot be made satisfactory by the investigator, the investigator should document the observed deficiencies in writing to the staff member's supervisor(s) and inform the sponsor. Depending on the severity of the deficiencies, the clinical trial may need to be voluntarily suspended until personnel can be replaced.

b. Parties Other than Study Staff

There are often critical aspects of a study performed by parties not involved directly in patient care or contact and not under the direct control of the clinical investigator. For example, clinical chemistry testing, radiologic assessments, and electrocardiograms are commonly done by a central independent facility retained by the sponsor. Under these arrangements, the central facility usually provides the test results directly to the sponsor and to the investigator. Because the activities of these parties are critical to the outcome of the study and because the sponsor retains the services of the facility, the sponsor is responsible for ensuring that these parties are competent to fulfill and are fulfilling their responsibilities to the study.

Less frequently, a study may require that investigators arrange to obtain information critical to the study that cannot be obtained at the investigator's site. For example, if the study protocol requires testing with special equipment or expertise not available at the investigator's site, the investigator might make arrangements for an outside facility to perform the test. In this case, the results are usually provided directly to the investigator, who then submits the information to the sponsor. If the investigator retains the services of a facility to perform study assessments, the investigator should take steps to ensure that the facility is adequate (e.g., has the required certification or licenses). The investigator may also institute procedures to ensure the integrity of data and records obtained from the facility providing the information (e.g., a process to ensure that records identified as coming from the facility are authentic and accurate). Procedures are particularly important when assessments are crucial to the evaluation of the efficacy or safety of an intervention or to the decision to include or exclude subjects who would be exposed to unreasonable risk.

Investigators should carefully review the reports from these external sources for results that are inconsistent with clinical presentation. To the extent feasible, and considering the specifics of study design, investigators should evaluate whether results appear reasonable, individually, and in aggregate, and they should document the evaluation. If investigators detect possible errors or suspect that results from a central laboratory or testing facility might be questionable, the investigator should contact the sponsor immediately.

c. Special Considerations for Medical Device Studies

Field clinical engineers (device sponsor employees) have traditionally played a role in some investigational device procedures (e.g., cardiology, orthopedics, and ophthalmology) by providing technical assistance to the device investigator. The field clinical engineer should be supervised by the investigator because the field clinical engineer's presence or activities may have the potential to bias

the outcome of studies, may affect the quality of research data, and/or may compromise the rights and welfare of human subjects. The field clinical engineer's activities should be described in the protocol. If the field engineer has face-to-face contact with subjects or if the activities of the field engineer directly affect the subject, those activities should also be described in the informed consent.

B. Protecting the Rights, Safety, and Welfare of Study Subjects

Investigators are responsible for protecting the rights, safety, and welfare of subjects under their care during a clinical trial (21 CFR 312.60 and 812.100). This responsibility should include:

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

The investigator should inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and the subject agrees to the primary physician being informed.

1. Reasonable Medical Care Necessitated by Participation in a Clinical Trial

During a subject's participation in a trial, the investigator (or designated subinvestigator) should ensure that reasonable medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the trial participation. If the investigator does not possess the expertise necessary to provide the type of medical care needed by a subject, the investigator should make sure that the subject is able to obtain the necessary care from a qualified practitioner. For example, if the study involves placement of a carotid stent by an interventional neuroradiologist and the subject suffers a cerebral stroke, the neuroradiologist should assess the clinical status of the subject and arrange for further care of the subject by a neurologist. Subjects should receive appropriate medical evaluation and treatment until resolution of any emergent condition related to the study intervention that develops during or after the course of their participation in a study, even if the follow-up period extends beyond the end of the study at the investigative site.

The investigator should also inform a subject when medical care is needed for conditions or illnesses unrelated to the study intervention or the disease or condition under study when such condition or illness is readily apparent or identified through the screening procedures and eligibility criteria for the study. For example, if the investigator determines that the subject has had an exacerbation of an existing condition unrelated to the investigational product or the disease or condition under study, the investigator should inform the subject. The subject should also be advised to seek appropriate care from the physician who was treating the illness prior to the study, if there is one, or assist the subject in obtaining needed medical care.

2. Reasonable Access to Medical Care

Investigators should be available to subjects during the conduct of the trial for medical care related to participation in the study. Availability is particularly important when subjects are receiving a drug that has significant toxicity or abuse potential. For example, if a study drug has potentially fatal toxicity, the investigator should be readily available by phone or other electronic communication 24 hours a day and in reasonably close proximity to study subjects (e.g., not in another state or on prolonged travel). Study subjects should be clearly educated on the possible need for such contact and on precisely how to obtain it, generally by providing pertinent phone numbers, e-mail addresses, and other contact information, in writing. Prior to undertaking the conduct of a study, prospective investigators should consider whether they can be available to the extent needed given the nature of the trial.

During any period of unavailability, the investigator should delegate responsibility for medical care of study subjects to a specific qualified physician who will be readily available to subjects during that time (in the manner a physician would delegate responsibility for care in clinical practice). If the investigator is a non-physician, the investigator should make adequate provision for any necessary medical care that the investigator is not qualified to provide.

3. Protocol Violations that Present Unreasonable Risks

There are occasions when a failure to comply with the protocol may be considered a failure to protect the rights, safety, and welfare of subjects because the non-compliance exposes subjects to unreasonable risks. For example, failure to adhere to inclusion/exclusion criteria that are specifically intended to exclude subjects for whom the study drug or device poses unreasonable risks (e.g., enrolling a subject with decreased renal function in a trial in which decreased function is exclusionary because the drug may be nephrotoxic) may be considered failure to protect the rights, safety, and welfare of the enrolled subject. Similarly, failure to perform safety assessments intended to detect drug toxicity within protocol-specified time frames (e.g., CBC for an oncology therapy that causes neutropenia) may be considered failure to protect the rights, safety, and welfare of the enrolled subject. Investigators should seek to minimize such risks by adhering closely to the study protocol.

ATTACHMENT A: COPY OF FORM 1572

DEPARTMENT OF HEALTH AND HUMAN SERVICES **FOOD AND DRUG ADMINISTRATION** **STATEMENT OF INVESTIGATOR** ***(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)*** (See instructions on reverse side.)	Form Approved: OMB No. 0910-0014. Expiration Date: May 31, 2009. *See OMB Statement on Reverse.* **NOTE:** No investigator may participate in an investigation until he/she provides the sponsor with a completed, signed Statement of Investigator, Form FDA 1572 (21 CFR 312.53(c)).

1. NAME AND ADDRESS OF INVESTIGATOR

2. EDUCATION, TRAINING, AND EXPERIENCE THAT QUALIFIES THE INVESTIGATOR AS AN EXPERT IN THE CLINICAL INVESTIGATION OF THE DRUG FOR THE USE UNDER INVESTIGATION. ONE OF THE FOLLOWING IS ATTACHED.

____CURRICULUM VITAE ____OTHER STATEMENT OF QUALIFICATIONS

3. NAME AND ADDRESS OF ANY MEDICAL SCHOOL, HOSPITAL OR OTHER RESEARCH FACILITY WHERE THE CLINICAL INVESTIGATIONS(S) WILL BE CONDUCTED

4. NAME AND ADDRESS OF ANY CLINICAL LABORATORY FACILITIES TO BEUSED IN THE STUDY.

5. NAME AND ADDRESS OF THE INSTITUTIONAL REVIEW BOARD (IRB) THAT IS RESPONSIBLE FOR REVIEW AND APPROVAL OF THE INVESTIGATION(S)

6. NAMES OF THE SUBINVESTIGATORS *(e.g., research fellows, residents, associates)* WHO WILL BE ASSISTING THE INVESTIGATOR IN THE CONDUCT OF THE INVESTIGATION(S)

.

7. NAME AND CODE NUMBER, IF ANY, OF THE PROTOCOL(S) IN THE IND FOR THE STUDY(IES) TO BE CONDUCTED BY THE INVESTIGATOR.

8. ATTACH THE FOLLOWING CLINICAL PROTOCOL INFORMATION:

FOR PHASE 1 INVESTIGATIONS, A GENERAL OUTLINE OF THE PLANNED INVESTIGATION INCLUDING THE ESTIMATED DURATION OF THE STUDY AND THE MAXIMUM NUMBER OF SUBJECTS THAT WILL BE INVOLVED.

FOR PHASE 2 OR 3 INVESTIGATIONS, AN OUTLINE OF THE STUDY PROTOCOL INCLUDING AN APPROXIMATION OF THE NUMBER OF SUBJECTS TO BE TREATED WITH THE DRUG AND THE NUMBER TO BE EMPLOYED AS CONTROLS, IF ANY; THE CLINICAL USES TO BE INVESTIGATED; CHARACTERISTICS OF SUBJECTS BY AGE, SEX, AND CONDITION; THE KIND OF CLINICAL OBSERVATIONS AND LABORATORY TESTS TO BE CONDUCTED; THE ESTIMATED DURATION OF THE STUDY; AND COPIES OR A DESCRIPTION OF CASE REPORT FORMS TO BE USED.

9. COMMITMENTS:

I agree to conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, rights, or welfare of subjects.

I agree to personally conduct or supervise the described investigation(s).

I agree to inform any patients, or any persons used as controls, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent in 21 CFR Part 50 and institutional review board (IRB) review and approval in 21 CFR Part 56 are met.

I agree to report to the sponsor adverse experiences that occur in the course of the investigation(s) in accordance with 21 CFR 312.64.

I have read and understand the information in the investigator's brochure, including the potential risks and side effects of the drug.
I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments.

I agree to maintain adequate and accurate records in accordance with 21 CFR 312.62 and to make those records available for inspection in accordance with 21 CFR 312.68.

I will ensure that an IRB that complies with the requirements of 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation.

I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others.

Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in 21 CFR Part 312.

INSTRUCTIONS FOR COMPLETING FORM FDA 1572
STATEMENT OF INVESTIGATOR:

1. Complete all sections. Attach a separate page if additional space is needed.
2. Attach curriculum vitae or other statement of qualifications as described in Section 2.
3. Attach protocol outline as described in Section 8.
4. Sign and date below.
5. FORWARD THE COMPLETED FORM AND ATTACHMENTS TO THE SPONSOR. The sponsor will incorporate this information along with other technical data into an Investigational New Drug Application (IND).

INVESTIGATORS SHOULD NOT SEND THIS FORM DIRECTLY TO THE FOOD AND DRUG ADMINISTRATION.

10. SIGNATURE OF INVESTIGATOR	11. DATE

(**WARNING:** A willfully false statement is a criminal offense U.S.C. Title 18, Sec. 1001.)

Public reporting burden for this collection of information is estimated to average 100 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research Central Document Room 5901-B Ammendale Road Beltsville, MD 20705-1266	Department of Health and Human Services Food and Drug Administration Center for Biologics Evaluation and Research (HFM-99) 1401 Rockville Pike Rockville, MD 20852-1448	"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number." "

Please DO NOT RETURN this application to this address.

ATTACHMENT B: INVESTIGATOR RESPONSIBILITIES FOR SIGNIFICANT RISK DEVICE INVESTIGATIONS

This document is intended to assist investigators in identifying and complying with their responsibilities in connection with the conduct of clinical investigations involving medical devices. Although this guidance primarily addresses duties imposed upon clinical investigators by regulations of the Food and Drug Administration (FDA), investigators should be cognizant of additional responsibilities that may derive from other sources (such as the study protocol itself, the investigator agreement, any conditions of approval imposed by FDA or the governing institutional review board, as well as institutional policy and state law).

GENERAL RESPONSIBILITIES OF INVESTIGATORS (21 CFR 812.100)

1. Ensuring that the investigation is conducted according to the signed agreement, the investigational plan, and applicable FDA regulations

2. Protecting the rights, safety, and welfare of subjects under the investigator's care

3. Controlling devices under investigation

4. Ensuring that informed consent is obtained from each subject in accordance with 21 CFR Part 50 and that the study is not commenced until FDA and IRB approvals have been obtained.

SPECIFIC RESPONSIBILITIES OF INVESTIGATORS (21 CFR 812.110)

1. Awaiting IRB approval and any necessary FDA approval before requesting written informed consent or permitting subject participation

2. Conducting the investigation in accordance with:

    a. The signed agreement with the sponsor
    b. The investigational plan
    c. The regulations set forth in 21 CFR Part 812 and all other applicable FDA regulations
    d. Any conditions of approval imposed by an IRB or FDA

3. Supervising the use of the investigational device. An investigator shall permit an investigational device to be used only with subjects under the investigator's supervision. An investigator shall not supply an investigational device to any person not authorized under 21 CFR Part 812 to receive it.

4. Disposing of the device properly. Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator shall return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.

MAINTAINING RECORDS (21 CFR 812.140)

An investigator shall maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:

1. Correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA

2. Records of receipt, use or disposition of a device that relate to:

    a. The type and quantity of the device, dates of receipt, and batch numbers or code marks
    b. Names of all persons who received, used, or disposed of each device
    c. The number of units of the device returned to the sponsor, repaired, or otherwise disposed of, and the reason(s) therefore

3. Records of each subject's case history and exposure to the device, including:

    a. Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent
    b. All relevant observations, including records concerning adverse device effects (whether anticipated or not), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests;
    c. A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.

4. The protocol, with documents showing the dates of and reasons for each deviation from the protocol

5. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation

INSPECTIONS (21 CFR 812.145)

Investigators are required to permit FDA to inspect and copy any records pertaining to the investigation including, in certain situations, those which identify subjects.

SUBMITTING REPORTS (21 CFR 812.150)

An investigator shall prepare and submit the following complete, accurate, and timely reports:

1. To the sponsor and the IRB:

- Any *unanticipated adverse device effect* occurring during an investigation. (Due no later than 10 working days after the investigator first learns of the effect.)
- *Progress reports* on the investigation. (These reports must be provided at regular intervals, but in no event less often than yearly. If there is a study monitor, a copy of the report should also be sent to the monitor.)
- Any *deviation from the investigational plan* made to protect the life or physical well-being of a subject in an emergency. (Report is due as soon as possible but no later than 5 working days after the emergency occurs. Except in emergency situations, a protocol deviation requires prior sponsor approval; and if the deviation may affect the scientific soundness of the plan or the rights, safety, or welfare of subjects, prior FDA and IRB approval are required.)
- Any use of the device *without obtaining informed consent*. (Due within 5 working days after such use.)
- A *final report.* (Due within 3 months following termination or completion of the investigation or the investigator's part of the investigation. For additional guidance, see the discussion under the section entitled "Annual Progress Reports and Final Reports.")
- *Any further information* requested by FDA or the IRB about any aspect of the investigation.

2. To the Sponsor:

- *Withdrawal of IRB approval* of the investigator's part of an investigation. (Due within 5 working days of such action).

INVESTIGATIONAL DEVICE DISTRIBUTION AND TRACKING

The IDE regulations prohibit an investigator from providing an investigational device to any person not authorized to receive it (21 CFR 812.110(c)). The best strategy for reducing the risk that an investigational device could be improperly dispensed (whether purposely or inadvertently) is for the sponsor and the investigators to closely monitor the shipping, use, and final disposal of devices. Upon completion or termination of a clinical investigation (or the investigator's part of an investigation), or at the sponsor's request, an investigator is required to return to the sponsor any remaining supply of the device or otherwise to dispose of the device as the sponsor directs (21 CFR 812.110(e)). Investigators must also maintain complete, current, and accurate records of the receipt, use, or disposition of investigational devices (21 CFR 812.140(a)(2)). Specific recordkeeping requirements are set forth at 21 CFR 812.140(a).

PROHIBITION OF PROMOTION AND OTHER PRACTICES (21 CFR 812.7)

The IDE regulations prohibit the promotion and commercialization of a device that has not been first cleared or approved for marketing by FDA. This prohibition is applicable to sponsors and investigators (or any person acting on behalf of a sponsor or investigator) and encompasses the following activities:

1. Promotion or test marketing of the investigational device

2. Charging subjects or investigators for the device a price larger than is necessary to recover the costs of manufacture, research, development, and handling

3. Prolonging an investigation beyond the point needed to collect data required to determine whether the device is safe and effective

4. Representing that the device is safe or effective for the purposes for which it is being investigated

Information Sheet Guidance for Sponsors, Clinical Investigators, and IRBs

Frequently Asked Questions – Statement of Investigator (Form FDA 1572)

U.S. Department of Health and Human Services
Food and Drug Administration
Office of Good Clinical Practice
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
May 2010

Procedural ***Contains Nonbinding Recommendations***

Information Sheet Guidance for Sponsors, Clinical Investigators, and IRBs Frequently Asked Questions – Statement of Investigator (Form FDA 1572)

Additional copies are available from:
Office of Good Clinical Practice
Office of the Commissioner
http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm
and/or
Office of Communications
Division of Drug Information, WO51, Room 2201
10903 New Hampshire Ave.
Silver Spring, MD 20993
Phone: 301-796-3400; Fax: 301-847-8714
druginfo@fda.hhs.gov
http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm
and/or
Office of Communication, Outreach and
Development, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Rockville, MD 20852-1448
http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm
(Tel) 800-835-4709 or 301-827-1800

U.S. Department of Health and Human Services
Food and Drug Administration
Office of Good Clinical Practice
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

May 2010

Procedural *Contains Nonbinding Recommendations*

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Information Sheet Guidance
For Sponsors, Clinical Investigators, and IRBs[17]
Frequently Asked Questions
Statement of Investigator (Form FDA 1572)

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

This guidance is intended to assist sponsors, clinical investigators, and institutional review boards (IRBs) involved in clinical investigations of investigational drugs and biologics. This guidance applies to clinical investigations conducted under 21 CFR Part 312 (Investigational New Drug Applications or IND regulations). It describes how to complete the Statement of Investigator form (Form FDA 1572).

The Food and Drug Administration (FDA or agency) has received a number of questions about Form FDA 1572. The most frequently asked questions are answered below. If you do not see your question answered here, you may submit it to gcp.questions@fda.hhs.gov or druginfo@fda.hhs.gov .

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

I. GENERAL

1. What is the Statement of Investigator, Form FDA 1572?

The Statement of Investigator, Form FDA 1572 (1572), is an agreement signed by the investigator to provide certain information to the sponsor and assure that he/she will comply with FDA regulations related to the conduct of a clinical investigation of an investigational drug or biologic. The most recent version of the 1572 is available online at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf

[17] This guidance document was developed by the Office of Good Clinical Practice in cooperation with the Agency's Center for Drug Evaluation and Research and Center for Biologics Evaluation and Research.

2. Why does this form need to be completed by an investigator?

The 1572 has two purposes: 1) to provide the sponsor with information about the investigator's qualifications and the clinical site that will enable the sponsor to establish and document that the investigator is qualified and the site is an appropriate location at which to conduct the clinical investigation, and 2) to inform the investigator of his/her obligations and obtain the investigator's commitment to follow pertinent FDA regulations. Investigators should complete the form as accurately as they can. Investigators should be aware that making a willfully false statement is a criminal offense under 18 U.S.C. 1001. Further, submission of a deliberately false statement to the sponsor or to the agency can be taken into consideration in a disqualification proceeding.

3. When must this form be completed and signed by an investigator?

Whenever a sponsor selects a new investigator to participate in a clinical investigation that is being conducted under an investigational new drug application (IND), the sponsor must obtain a completed and signed 1572 before permitting the investigator to begin participation in the clinical investigation (21 CFR 312.53(c)). The investigator should sign the form only after being given enough information to be informed about the clinical investigation and to understand the commitments described in Section #9 of the 1572. Having enough information about the study typically means that the investigator has received copies of, has read, and understands the protocol and investigator's brochure (if required[18]), and is familiar with the regulations governing the conduct of clinical studies.

The investigator's signature on this form constitutes the investigator's affirmation that he or she is qualified to conduct the clinical investigation and constitutes the investigator's written commitment to abide by FDA regulations in the conduct of the clinical investigation.

4. Must the investigator be a physician?

The regulations do not require that the investigator be a physician. Sponsors are required to select only investigators qualified by training and experience as appropriate experts to investigate the drug (21 CFR 312.53(a)). In the event the clinical investigator is a non-physician, a qualified physician (or dentist, when appropriate) should be listed as a subinvestigator for the trial and should be responsible for all trial-related medical (or dental) decisions. (ICH E6 section 4.3.1; http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073122.pdf).

[18] See 21 CFR 312.55; a study initiated by a sponsor-investigator is not required to have an investigator's brochure.

5. What are the minimum qualifications of an investigator?

As stated in #4, the regulations require that sponsors select investigators who are qualified by training and experience as appropriate experts to investigate the drug. The regulations do not specify the minimum requirements nor do the regulations specify what qualifications an investigator must have in order to be considered qualified by training and experience to conduct a clinical investigation. Sponsors have discretion in determining what qualifications, training, and experience will be needed, based on the general recognition that this would include familiarity with human subject protection (HSP) regulations (i.e., 21 CFR Parts 50 and 56) and practices as well as good clinical practice (GCP) regulations (see 21 CFR Part 312) and standards (e.g., ICH E6) for the conduct of clinical studies.

6. Does the 1572 need to be submitted to FDA?

No. Although the sponsor is required to collect the 1572 from the investigator, FDA does not require the form to be submitted to the agency. Many sponsors submit the 1572 to FDA, however, because it collects, in one place, information that must be submitted to FDA under 21 CFR 312.23(a)(6)(iii)(b).

7. When must a 1572 be updated or a new 1572 completed and signed by an investigator to reflect new or changed information?

There are two instances when it is necessary for an investigator to complete and sign a new 1572: when an investigator is participating in a new protocol that has been added to the IND and when a new investigator is added to the study (21 CFR 312.53(c)).
If there are other changes to information contained on a signed and dated 1572 (e.g., an IRB address change, the addition of new subinvestigators, the addition of a clinical research lab), the investigator should document the changes in the clinical study records and inform the sponsor of these changes, so that the sponsor can appropriately update the IND. The 1572 itself does not need to be revised and a new 1572 need not be completed and signed by the investigator. The sponsor can accumulate certain changes and submit this information to the IND in, for example, an information amendment or a protocol amendment.

8. If a clinical investigation is not conducted under an IND or is for a medical device, must investigators sign a 1572?

No. Under the regulations, a 1572 is only required for studies of investigational drugs and biologics conducted under an IND. It is not required for studies that are not done under an IND, and is not applicable to investigational device studies. Sponsors of device studies must obtain a signed investigator agreement (containing information similar to that requested on the 1572) from each participating investigator, per 21 CFR 812.43(c).

9. Must a sponsor conduct a foreign clinical study under an IND?

No. A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived (see #12 and #13 below). When the foreign clinical study is not conducted under an IND, the sponsor must ensure that this study complies with 21 CFR 312.120, "Foreign clinical studies not conducted under an IND," if the sponsor intends to submit the study to FDA to support clinical investigations conducted in the United States and/or marketing approval. An application based solely on foreign clinical data must meet criteria listed in 21 CFR 314.106.

10. Must investigators who conduct studies outside of the United States sign a 1572?[19]

If a foreign clinical study is conducted under an IND, then all FDA IND regulations, including the requirement to obtain a signed 1572, must be met. If a clinical study is conducted outside of the U.S. and is not conducted under an IND, then the investigator need not sign a 1572. If local laws or regulations prohibit the signing of a 1572, FDA would expect the sites to operate as non-IND sites and the study conducted as a non-IND study. If the study data is to be submitted to support a marketing application (e.g., a new drug application (NDA)), the study must be conducted in compliance with 21 CFR 312.120.

11. If a foreign clinical study is being conducted under an IND, what are the investigator's responsibilities with respect to local laws and regulations?

Investigators are responsible for complying with the applicable laws and regulations of the country in which the study is being conducted, regardless of whether the study is being conducted under an IND. We recommend that sponsors obtain signed, written statements from investigators acknowledging their commitment to comply with local laws and requirements. In addition, if a foreign clinical study is being conducted under an IND, the investigator must sign Form FDA 1572 (investigator statement) and ensure that the study is conducted in accordance with the investigator statement and all other applicable regulations under 21 CFR Part 312.

12. For foreign clinical studies conducted under an IND, how can an investigator sign the 1572 when the investigator knows he/she cannot commit to all of the requirements on the form, specifically IRB membership (21 CFR 56.107)?

IRB review and approval is required before a clinical study can be initiated under an IND (21 CFR 56.103(a)). FDA may waive any of the IRB requirements for specific research activities or for classes of research activities otherwise covered by the IRB regulations (21 CFR 56.105), but FDA uses the waiver provision only when alternative mechanisms for ensuring protection of the rights and welfare of human subjects are acceptable. The most common circumstance for which FDA receives a waiver request is when a sponsor wishes to conduct a foreign clinical study under an IND. In this case, typically an Independent Ethics Committee (IEC) that operates in accordance with Good Clinical

[19] Investigators conducting studies outside of the U.S. may want to consult with local regulatory authorities for additional guidance when considering whether to conduct studies under an IND.

Practice (GCP) is utilized instead of a U.S. IRB. Although its membership and functions for assuring human subject protection are comparable to an IRB, an IEC may not meet all of the IRB requirements contained in 21 CFR Part 56.

For a foreign study, an IRB waiver request should contain a description of alternative mechanisms for assuring human subject protection. It would generally be acceptable for a waiver request to state the intention to use an IEC that complies with GCP (e.g., ICH E6) instead of an IRB that complies with 21 CFR Part 56.

The sponsor should submit the waiver request to the IND under which the study will be conducted. The IND will have been submitted to the appropriate review division in either the Center for Drug Evaluation and Research (CDER) or the Center for Biologics Evaluation and Research (CBER). The sponsor will be informed by the agency in writing whether the waiver request is denied or granted. If a waiver is granted, the sponsor should have investigators attach a copy of the letter granting the waiver to the signed 1572 in the investigator's record.

13. If a sponsor chooses to conduct a foreign clinical study (or operate non-US sites in a multinational study) under an IND and the investigators at these non-US sites comply with the ICH E6 Good Clinical Practice Consolidated Guidance, would the non-US investigators also be in compliance with FDA's IND requirements under 21 CFR Part 312?

Yes, with two exceptions. The first is that the FDA requirements for IRBs under 21 CFR Part 56 are slightly different with respect to membership and function. To address this issue, as described in #12 above, FDA can provide a specific waiver from the Part 56 IRB requirements, allowing an IEC that complies with good clinical practice to substitute for the IRB.[20] The second exception is that the requirements for informed consent under 21 CFR Part 50 for particular clinical trials (e.g., emergency research under 21 CFR 50.24, clinical investigations involving pediatric subjects under Subpart D) are more extensive with respect to IRB responsibilities. Because these types of trials are uncommon, our experience has not revealed that this has caused a conflict; but in the event of one, we would be willing to discuss a resolution with the sponsor on a case-by-case basis. If the investigator or sponsor believes that there are other conflicting requirements, the sponsor may request a waiver from FDA from the specific requirement under 21 CFR 312.10.

Contains Nonbinding Recommendations

[20] [4] See "Information Sheet Guidance for Sponsors, Clinical Investigators, and IRBs: Waiver of IRB Requirements for Drug and Biological Product Studies," January 2006, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM080613.pdf.

14. Must foreign clinical study sites in a multinational study that includes domestic sites be conducted under an IND?

No. A multinational study may include domestic sites under the IND and foreign sites not under the IND. Investigational drug and biologics studies conducted in the U.S. must be conducted in compliance with the IND requirements contained in 21 CFR 312, which includes the requirement that investigators sign the 1572. If a study also involves foreign clinical sites, the sponsor may choose, but is not required, to include the foreign clinical sites under the IND. The investigators from the U.S. sites and any foreign sites included under the IND would be required to sign the 1572. The investigators from the foreign sites that are not included under the IND are not required to sign the 1572.

If the sponsor chooses to conduct a multinational study with U.S. and some foreign sites under the IND, and other foreign sites not under the IND, the sponsor can submit a single protocol to the IND and all sites would follow this protocol. Alternatively, the sponsor can conduct a multinational study with one protocol for sites under the IND (U.S. sites and some foreign sites) and a different protocol(s) for foreign sites not under the IND. If the intent is to pool the data from U.S. and foreign sites, the protocols would ordinarily be very similar or identical. The U.S. sites and any foreign sites included under the IND must follow the protocol that was submitted to the IND. For foreign sites that are not included under the IND, the protocol(s) does not need to be submitted to the IND. In general, if the sponsor intends to submit the data in an application for marketing approval, we recommend that the sponsor identify the foreign sites that will not be conducted under the IND and discuss plans to pool the data from U.S. and foreign sites with the appropriate FDA review division.

Note, however, that 21 CFR 312.32(b) requires sponsors to promptly review information about the safety of the investigational drug obtained or otherwise received by the sponsor from any source, foreign or domestic. Under 21 CFR 312.32(c), sponsors must also notify FDA and all participating investigators in an IND safety report of any adverse experience associated with the use of the drug that is both serious and unexpected. This means that FDA and all participating investigators under the IND would be informed of such an adverse experience, even if it occurred in a foreign study not conducted under the IND.

15. How does a sponsor submit information to FDA about a foreign clinical study that was not conducted under an IND?

Under 21 CFR 312.120, the sponsor can submit information to FDA from a foreign clinical study that was not conducted under an IND to support clinical investigations in the United States and/or marketing approval. When submitting information about a foreign clinical study, it is helpful to clearly identify in the cover letter that the material is being submitted in accordance with 21 CFR 312.120. The submission requirements for supporting documentation can be found at 21 CFR 312.120(b).

16. Should a new form be prepared and signed when the OMB expiration date is reached?

No. There is no need to prepare and sign a new 1572 when the OMB expiration date has been reached.

17. Does FDA expect a double-sided 1572, or is a two-page document printed from the FDA website acceptable?

Either is acceptable; however, FDA recommends that a two-page document be stapled so that there is no question about what form the investigator signed.

18. How should the 1572 be completed?

The 1572 on FDA's website may be completed by typing the information directly into the fillable form and printing the completed form. Alternatively, it is acceptable to print the blank form from FDA's website and hand-write or type the information onto the form. Typed forms are preferable because they are usually more legible. The completed form must be signed and dated by the investigator (either by hand or using an acceptable electronic method).

II. SECTION #1: NAME AND ADDRESS OF INVESTIGATOR

19. How should an investigator's name appear on the 1572?

Section #1 should contain the investigator's full legal name (e.g., name on the investigator's birth certificate or marriage certificate). Titles, degrees, and/or professional qualifications may follow the investigator's legal name, if desired.

20. What address should be entered into Section #1?

The address where the investigator can be reached by mail or in person should be entered in Section #1 of the 1572. Usually, this corresponds to the investigator's work or business address.

21. Should co-investigators be listed on the 1572 in Section #1? Is it acceptable to have more than one investigator at a single site?

The term co-investigator is not defined in FDA regulations. As commonly used, the term is meant to indicate that each co-investigator is fully responsible for fulfilling all of the obligations of an investigator as identified in 21 CFR 312.60. Thus under 21 CFR 312.3(b), each co-investigator is an investigator, and as such must sign a separate 1572.

In some situations, it is preferable to have more than one investigator responsible for a clinical investigation. For example, when a study is conducted at multiple research facilities that are not in close proximity, FDA expects an investigator who has signed a

1572 to be available at each location to either personally conduct or supervise the study. This responsibility cannot be delegated to a subinvestigator.

Although not necessary, it is acceptable to have more than one investigator at a single site. For example, the conduct and supervision of a large investigation with many subjects or complicated procedures might be shared among several investigators, each of whom has signed a 1572 when the investigation is conducted under an IND. This is distinct from a subinvestigator (see #31) whose role in the clinical investigation is more limited.

III. SECTION #2: EDUCATION, TRAINING, AND EXPERIENCE THAT QUALIFY THE INVESTIGATOR AS AN EXPERT IN THE CLINICAL INVESTIGATION

22. What is the purpose of Section #2?

Section #2 requires the investigator to attach a curriculum vitae (CV) or other statement of qualifications, showing the education, training and experience that qualifies the investigator as an expert in the clinical investigation of the drug/biologic for the use under investigation. Information identified in this section and attached to the 1572 enables the sponsor to assess an investigator's qualifications.

23. Does the CV or other statement of qualifications need to be updated during a clinical study?

No. FDA regulations do not require a CV or other statement of qualifications to be updated during a clinical study.

24. Are CVs required to be signed and dated?

No. FDA regulations do not require a CV to be signed and dated. The investigator's dated signature on the 1572 is sufficient to attest to the accuracy of the CV or other statement of qualifications submitted with the 1572.

IV. SECTION #3: NAME AND ADDRESS OF ANY MEDICAL SCHOOL, HOSPITAL, OR OTHER RESEARCH FACILITY WHERE THE CLINICAL INVESTIGATION(S) WILL BE CONDUCTED

25. What address(es) should be entered in Section #3?

The address(es) of the location(s) where the investigation will be conducted and to where the test articles will be shipped, if different from the investigator's address of record, should be entered in Section #3.

26. What qualifies as a research facility for Section #3?

Section #3 is intended to identify facilities where study activities will be conducted and clinical data will be generated or collected. This includes facilities where subjects will be seen and study procedures performed. For example, this might include locations such as health care facilities where the test article will be administered, or where physical exams will be performed. Facilities where other important clinical investigation functions are performed may also be identified in Section #3. For example, a research laboratory where the test article is prepared, a special storage facility where the test article will be kept, or a location where tissue specimens are collected should be listed in this section.

27. If an investigator sees study subjects at more than one site, should the investigator list all sites on the 1572?

Yes. The names and addresses of each of the study sites should be identified in Section #3. However, if the protocol specifies that the investigative product can be administered at a subject's home (for example, the protocol allows for daily injections to be administered by a registered nurse in the subject's home), the subjects' home addresses do not have to be listed on the 1572. Study records should reflect that the test article was administered at subjects' homes per the protocol.

V. SECTION #4: NAME AND ADDRESS OF CLINICAL LABORATORY FACILITIES TO BE USED IN THIS STUDY

28. What qualifies as a clinical laboratory facility for Section #4?

Section #4 is intended to identify clinical laboratories or testing facilities directly contributing to or supporting the clinical study (for example, diagnostic labs performing blood work, imaging centers, cardiology labs, etc.). This may include analytical labs that provide pharmacokinetic analysis, and laboratories supplying efficacy data for clinical investigations conducted under an IND.

29. If a laboratory is sending samples to satellite or other contract labs for additional testing, should these labs be identified in Section #4?

It is only necessary to list the primary laboratory, provided that laboratory can trace the samples to each of the satellite and/or contract labs where the tests were performed.

VI. SECTION #5: NAME AND ADDRESS OF THE INSTITUTIONAL REVIEW BOARD (IRB) RESPONSIBLE FOR THE REVIEW AND APPROVAL OF THE STUDY(IES)

30. Does the IRB reviewing and approving the clinical study have to be at the same location as where the research is conducted?

The regulations permit review of research by IRBs at locations other than where the research is being performed (e.g. independent or non-institutional IRB; use of a cooperative IRB review process; see 21 CFR 56.114). Therefore an IRB may review clinical studies that are not performed on-site as long as requirements in 21 CFR Parts 50 and 56 are met. For more information on cooperative research arrangements, see the FDA Guidance for Industry-Using a Centralized IRB Review Process in Multicenter Clinical Trials (http://www.fda.gov/RegulatoryInformation/Guidances/ucm127004.htm).

VII. SECTION #6: NAMES OF THE SUBINVESTIGATORS WHO WILL BE ASSISTING THE INVESTIGATOR IN THE CONDUCT OF THE INVESTIGATION(S)

31. Who should be listed as a subinvestigator in Section #6?

FDA's regulation at 21 CFR 312.3(b) states: "In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. 'Subinvestigator' includes any other individual member of that team." 21 CFR 312.53(c)(1)(viii) requires the investigator to provide "a list of the names of the subinvestigators (e.g., research fellows, residents) who will be assisting the investigator in the conduct of the investigation(s)."

The purpose of Section #6 is to capture information about individuals who, as part of an investigative team, will assist the investigator and make a direct and significant contribution to the data. The decision to list an individual in Section #6 depends on his/her level of responsibility (i.e., whether he/she is performing significant clinical investigation-related duties). In general, if an individual is directly involved in the performance of procedures required by the protocol, and the collection of data, that person should be listed on the 1572. For example, if the protocol notes that each subject needs to visit a specified internist who will perform a full physical to qualify subjects for the clinical investigation, that internist should be listed in Section #6.

32. ***Should research nurses, other nurses, residents, fellows, office staff, or other hospital staff be listed in Section #6?***

Hospital staff, including nurses, residents, or fellows and office staff who provide ancillary or intermittent care but who do not make a direct and significant contribution to the clinical data, do not need to be listed individually. It is not necessary to include in this section a person with only an occasional role in the conduct of the research, e.g., an on-call physician who temporarily dealt with a possible adverse effect or a temporary substitute for any research staff (see ICH E3, Section 6) (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073113.pdf).

Concerning staff residents on rotation, it may be difficult to prospectively identify those individuals who might perform specified protocol procedures or collect clinical data. Specific names of the rotational staff do not have to be listed in Section #6. Instead, to successfully address this scenario, the names of rotational individuals and the procedures they are expected to perform should be included in the clinical study records. This information should also be sent to the sponsor for submission to FDA in, for example, an information amendment.

33. Should pharmacists or research coordinators be listed in Section #6?

The decision about whether to list a pharmacist or research coordinator on the 1572 is a matter of judgment, dependent upon the contribution that the individual makes to the study. For example, a research pharmacist may prepare test articles and maintain drug accountability for many clinical studies that are ongoing concurrently at an institution. Because the pharmacist would not be making a direct and significant contribution to the data for a particular study, it would not be necessary to list the pharmacist as a subinvestigator in Section #6, but he/she should be listed in the investigator's study records.

Generally, a research coordinator has a greater role in performing critical study functions and making direct and significant contributions to the data. For example, a research coordinator often recruits subjects, collects and evaluates study data, and maintains study records. Therefore, the research coordinator should usually be listed in Section #6 of the 1572.

34. Is a statement of qualifications required for subinvestigators?

No. The regulations at 21 CFR 312.53(c)(1)(viii) require only that subinvestigators' names be listed in Section #6 of the 1572. It is the responsibility of the sponsor to select investigators qualified by training and experience, as appropriate experts, to investigate the drug. The investigator must ensure that all associates, colleagues, and employees assisting with the conduct of the clinical investigation are aware of their obligations including complying with the IND regulations.

35. Do individuals who are listed in Section #6 on the 1572 have to submit information about their financial interests?

Yes. Under 21 CFR Part 54 (Disclosure of Financial Interests by Clinical Investigators), a person listed or identified as an investigator or subinvestigator who is directly involved in the treatment or evaluation of research subjects must submit financial disclosure information to the sponsor. For purposes of this financial disclosure regulation, the term investigator also includes the spouse and each dependent child of the investigator and subinvestigator. (21 CFR 54.2(d) and 54.4). For additional information about financial disclosure, see FDA's Guidance for Industry Financial Disclosure by Clinical Investigators (http://www.fda.gov/RegulatoryInformation/Guidances/ucm126832.htm)

VIII. SECTION #7: NAME AND CODE NUMBER, IF ANY, OF THE PROTOCOL(S) IN THE IND FOR STUDY(IES) TO BE CONDUCTED BY THE INVESTIGATOR

36. What information should be included in this section?

List the name and code number (if any) of all the protocols under the IND that will be conducted by the investigator signing the 1572. A code number is an identifying number assigned by the sponsor. As a reminder, some investigators may be responsible for submitting certain clinical trial information to the National Institutes of Health clinical trials data bank under 42 U.S.C. 282(j), 402(j) of the Public Health Service Act. Although not all investigators will be expected to meet this requirement, go to www.clinicaltrials.gov for further information about potential responsibilities.

IX. SECTION #8: CLINICAL PROTOCOL INFORMATION

37. How should Section #8 be completed for a phase 4 study?

Phase 4 refers to the timing of a clinical study (i.e., postmarketing) rather than the characteristics of the study, which are described under 21 CFR 312.21, Phases of an investigation. A postmarketing clinical trial would meet the description of a phase 2 or 3 investigation and a full protocol would be submitted. The investigator does not need to mark either of the boxes in Section #8, but should identify in Section #7 that the study is a phase 4 study.

38. Can an investigator submit the study protocol instead of an outline of the study protocol?

Yes. The protocol or a detailed description is required for any phase 2 or 3 clinical trial. Phase 1 studies can be supported by an outline (see 21 CFR 312.53).

Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies

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Guidance for Industry and Food and Drug Administration Staff

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The draft of this document was issued on November 10, 2011.

For questions regarding this document, contact CDRH's Andrew Farb, 301-796-6343, Andrew.Farb@fda.hhs.gov or Dorothy Abel, 301-796-6366, Dorothy.Abel@fda.hhs.gov, or CBER's Office of Communication, Outreach and Development at 1-800-835-4709 or 301-827-1800.

Preface

Public Comment

You may submit written comments and suggestions at any time for Agency consideration to the Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, rm. 1061, (HFA-305), Rockville, MD, 20852. Submit electronic comments to http://www.regulations.gov. Identify all comments with the docket number FDA-2011-D0787. Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

Additional copies are available from the Internet. You may also send an e-mail request to dsmica@fda.hhs.gov to receive an electronic copy of the guidance or send a fax request to 301-827-8149 to receive a hard copy. Please use the document number 1782 to identify the guidance you are requesting.

Additional copies of this guidance document are also available from the Center for Biologics Evaluation and Research (CBER) by written request, Office of Communication, Outreach, and Development (HFM-40), 1401 Rockville Pike, Rockville, MD 20852-1448, or by telephone, 1-800-835-4709 or 301-827-1800, or by e-mail at ocod@fda.hhs.gov, or from the Internet at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm.

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Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies

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Guidance for Industry and Food and Drug Administration Staff

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

1. Introduction

This document is intended to provide guidance to FDA staff, clinicians, medical device innovators, and industry on the development and review of Investigational Device Exemption (IDE) applications for early feasibility studies of significant risk devices.[1] Early feasibility studies allow for early clinical evaluation of devices to provide proof of principle and initial clinical safety data. These studies may be appropriate early in device development when clinical experience is necessary because nonclinical testing methods are not available or adequate to provide the information needed to advance the developmental process. As with all clinical studies, initiation of an early feasibility study must be justified by an appropriate benefit-risk analysis and adequate human subject protection measures.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should

[1] *Significant risk device* is defined at 21 CFR 812.3(m) as an investigational device that:
(1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; (2) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;

(3) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or

(4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

2. Regulatory Background

Section 520(g) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) [21 U.S.C. § 360j(g)] establishes a framework for FDA to grant devices for investigational use an exemption from certain requirements so that experts qualified by scientific training and experience can investigate their safety and effectiveness. This exemption is known as an Investigational Device Exemption (IDE). For significant risk devices, the sponsor must first submit an IDE application and obtain FDA approval.[2]

The FD&C Act expressly recognizes that information to be included in an IDE application may vary depending on the investigation. Section 520(g)(2)(C) states:

Procedures and conditions prescribed [for granting investigational device exemptions] may appropriately vary depending on:

· the scope and duration of clinical testing to be conducted under such exemption,

· the number of human subjects that are to be involved in such testing,

· the need to permit changes to be made in the device subject to the exemption during testing conducted in accordance with a clinical testing plan required under paragraph (3)(A) [in section 520(g) of the FD&C Act], and

· whether the clinical testing of such device is for the purpose of developing data to obtain approval for the commercial distribution of the device.

As with all clinical studies of investigational devices, an early feasibility study must comply with 21 CFR part 812, including the requirements outlined below:

· Application (21 CFR 812.20): explains when a sponsor must submit an IDE application and the information that the IDE application must contain, including the investigational plan and report of prior investigations.

· Investigational Plan (21 CFR 812.25): explains what information the Investigational Plan must contain, including the purpose of the investigation, the protocol, risk analysis, description of the device, monitoring procedures, labeling, consent materials, and information about the Institutional Review Boards (IRB) reviewing the investigation.

· Report of Prior Investigations (21 CFR 812.27): explains what information the Report of Prior Investigations must contain, including reports of all prior clinical, animal, and laboratory testing of the device.

· Supplemental applications (21 CFR 812.35): explains when changes to the device and Investigational Plan must have prior FDA approval and the appropriate manner to notify FDA of changes that do not require prior approval.

[2] 21 CFR 812.20(a).

Adopting the principles set forth in section 520(g)(2)(C) of the FD&C Act, Sections 5-8 of this guidance clarify how some of these requirements should be applied to early feasibility study IDEs.

3. Definitions and Scope

For the purposes of this guidance, clinical study types are defined as follows:[21]

- An **early feasibility study** is a limited clinical investigation of a device early in development, typically before the device design has been finalized, for a specific indication (e.g., innovative device for a new or established intended use, marketed device for a novel clinical application). It may be used to evaluate the device design concept with respect to initial clinical safety and device functionality in a small number of subjects (generally fewer than 10 initial subjects) when this information cannot practically be provided through additional nonclinical assessments or appropriate nonclinical tests are unavailable. Information obtained from an early feasibility study may guide device modifications. An early feasibility study does not necessarily involve the first clinical use of a device.
- A **first in human (FIH) study** is a type of study in which a device for a specific indication is evaluated for the first time in human subjects. This document only discusses FIH studies that meet the definition of an early feasibility study.
- A **traditional feasibility study** is a clinical investigation that is commonly used to capture preliminary safety and effectiveness information on a near-final or final device design to adequately plan an appropriate pivotal study. Because the study of a near-final or final device design takes place later in development than an early feasibility study, FDA would expect to see more nonclinical (or prior clinical) data in a traditional feasibility study IDE application.[22] A traditional feasibility study does not necessarily need to be preceded by an early feasibility study.
- A **pivotal study** is a clinical investigation designed to collect definitive evidence of the safety and effectiveness of a device for a specified intended use, typically in a

[21] In this guidance, the term 'feasibility' is considered synonymous with 'pilot.' For consistency purposes, 'feasibility' is the term that should be used in reference to the types of clinical studies that precede the pivotal study phase.

[22] Additional nonclinical testing could be completed concurrent with conducting the early feasibility study if needed to support the conduct of a traditional feasibility or pivotal study.

statistically justified number of subjects. It may or may not be preceded by an early and/or a traditional feasibility study.

Early feasibility studies may be conducted for multiple reasons, such as obtaining *initial* insights into:

- the clinical safety of the device-specific aspects of the procedure;
- whether the device can be successfully delivered, implanted or used;
- operator technique challenges with device use;
- human factors (e.g., difficulties in comprehending procedural steps);
- the clinical safety of the device (e.g., evaluation of device-related serious adverse events);
- whether the device performs its intended purpose (e.g., mechanical function, making intended measurements);
- device failures;
- patient characteristics that may impact device performance (e.g., anatomical limitations); and
- therapeutic parameters (e.g., energy applied, sizing, dose released) associated with device use.

Unlike traditional feasibility studies, which are focused on providing initial clinical safety and effectiveness information for a near final or final device design or capturing data to guide the development of a pivotal study, early feasibility studies have a broader purpose. Early clinical experience obtained from an early feasibility study increases the efficiency of the device development process, as it may be used to:

- identify appropriate modifications to the procedure or device;
- optimize operator technique;
- refine the intended use population;
- refine nonclinical test plans or methodologies; and • develop subsequent clinical study protocols.

To determine which type of clinical study (early feasibility, traditional feasibility, or pivotal) is appropriate to pursue, certain factors, such as the novelty of the device, its intended clinical use, the stability of the device design, and the amount of test data available to support the IDE application should be considered. An early feasibility study is appropriate when device changes are expected and when, due to the novelty of the device or its intended use, a clinical study is expected to provide information that cannot be practically obtained through additional nonclinical assessments. An early feasibility study may be appropriate even if a device or a prototype of the device has previously been used clinically for the intended clinical use. Note that not all novel devices or uses warrant an early feasibility study, nor would FDA mandate that an early feasibility study be conducted. A traditional feasibility study or a pivotal study may be more appropriate if the device design is near-final or final, respectively, depending on the amount of data available to justify the study. Prior to IDE submission and to avoid preventable

delays, it is advisable to contact FDA to determine whether the proposed investigation can be classified as an early feasibility study.

The guidance provided herein is specific to early feasibility study IDEs only and is not applicable to other types of clinical studies. As discussed above, excluded from the scope of this document are studies involving the first human use of a device that do not otherwise meet the definition of an early feasibility study. For example, the first human use of a non-innovative device for a well-understood clinical use could appropriately be evaluated under a traditional feasibility or a pivotal study rather than an early feasibility study.

4. Overview

FDA recognizes the value of encouraging medical device innovation to address clinical needs and improve patient care, particularly when alternative treatments or assessments are unavailable, ineffective, or associated with substantial risks to patient safety. This guidance has been developed to facilitate the early clinical evaluation of medical devices in the United States under the IDE regulations, using risk mitigation strategies that appropriately protect human subjects in early feasibility studies.

An early feasibility study IDE application must comply with section 520(g) of the FD&C Act [21 U.S.C. § 360j(g)] and 21 CFR part 812; however, the procedures and conditions prescribed for IDEs may vary depending on the type of clinical study (see Section 2).

This guidance outlines new policy regarding the application for and approval of early feasibility study IDEs. The essential elements of this policy are as follows:

1. FDA approval of an IDE application for an early feasibility study**,** including certain first in human studies**,** may be based on less nonclinical data than would be expected for a traditional feasibility or a pivotal study (see Section 5). This is because early feasibility studies are only appropriate when additional nonclinical testing would not provide the information needed to advance the developmental process. Identification of the data necessary to support an early feasibility study should be based on a thorough device evaluation strategy that describes the device procedure, performance, and basic safety-related attributes and addresses the potential failure modes (see Section 6.3). This policy is intended to facilitate initiation of clinical studies in the United States earlier in the device development process than has historically occurred.[23]

2. This guidance introduces new approaches to facilitate timely device and clinical protocol modifications during an early feasibility study (see Section 8), while still requiring compliance with the IDE regulations in 21 CFR part 812, as follows:

· more types of modifications that can be made under a 5-day notification without prior FDA approval, as compared with other types of studies;

[23] Note that this guidance does not recommend that sponsors prematurely initiate clinical testing when further useful and appropriate nonclinical testing can be performed for the particular device the sponsor is developing.

· a contingent approval process that permits changes contingent upon acceptable nonclinical test results without requiring additional FDA action; and · interactive review of IDE supplements and amendments.

This guidance document highlights and reviews key principles unique to an early feasibility study IDE with respect to the Report of Prior Investigations, the clinical protocol, risk mitigation strategies, and subject protection measures (see Sections 6 and 7).

Throughout this early feasibility study guidance, there are recommendations for sponsors to interact with FDA, utilizing the Pre-Submission (Pre-Sub) process to optimize the preparation and quality of early feasibility study IDE applications.[24] Appendix 1 summarizes the key elements for an early feasibility study Pre-Sub.[7]

This guidance is not intended to address all required elements of IDE applications or to provide a comprehensive tutorial on best clinical practices for investigational medical device studies. Furthermore, while this document outlines the general principles for preparing and reviewing early feasibility study IDE applications, it is not intended to provide guidance on the devicespecific nonclinical information needed to justify initiation of an early feasibility study, or the specific data required to progress to other phases of clinical study for a particular device type or clinical indication. It is recommended that discussions regarding justification for study initiation take place during the Pre-Sub process.

5. Targeting approval for an Early Feasibility Study IDE Application

Because there are differences in the amount and type of information that is needed for an early feasibility study as compared to a traditional feasibility or pivotal study, the IDE application should clearly state that the proposed study is an early feasibility study and provide justification for conducting this type of study. To improve the likelihood of IDE approval, the following questions should be addressed with supporting information in the original early feasibility study IDE application:

1. What is the clinical condition to be treated or assessed by the device?
2. What is the standard of care for the clinical condition and expected clinical outcomes associated with the standard of care?

3. What are the anticipated benefits associated with use of the study device?
4. Is the information included in the Report of Prior Investigations (Section 6) adequate to support initiation of the study?

[24] For more information on the Pre-Submission process, see FDA's draft guidance "Medical Devices: The PreSubmission Program and Meetings with FDA Staff"

5. Does the Investigational Plan include a thorough risk analysis, sufficient risk mitigation strategies, adequate human subject protection measures, and an appropriate clinical study protocol (see Section 7)?

6. Are the potential risks associated with the device use likely to be outweighed by the anticipated benefits of the early feasibility study, that is, is initiation of the clinical study justified based on the clinical need for the device, Report of Prior Investigations and Investigational Plan?

FDA may approve an investigation as proposed, approve it with conditions, or disapprove it.[8] FDA will generally disapprove an IDE if there is reason to believe that the foreseeable risks to the study subjects are not outweighed by the anticipated benefits to the subjects and the importance of the knowledge to be gained.[9]

prospective study subjects' tolerance for risk; risk mitigation strategies included in the clinical protocol; and information indicating that the device should perform as intended and catastrophic failure will not likely occur.

Early feasibility studies are designed to gain initial clinical insights when additional nonclinical testing methods are not available or adequate to provide the information needed to advance device development. These studies may be initiated before the design of the device is finalized and, in light of the early stage of device development and the small number of subjects, may be justified based on less evidence than for other types of clinical studies. As a result, they may carry greater unknown risk than traditional feasibility and pivotal studies. This makes human subject protection measures, such as adequate informed consent and IRB review, all the more important in an early feasibility study (see Section 7).[25] At the same time, benefits deriving from the knowledge to be gained may be substantial during the early phase of device development, particularly for innovative devices or intended uses. Even though early feasibility studies are not designed or intended to generate statistically valid results, they should be conducted for specified purpose(s), enroll the appropriate subjects, utilize meaningful endpoints, and capture relevant information so that the results can be used to further device development. Importantly, although early feasibility studies can begin before the design of the device is finalized, there still should be reason to believe that the device will function as intended.

Compared to a traditional feasibility or pivotal study, less nonclinical data would generally need to be included in the Report of Prior Investigations for an early feasibility study IDE application. For example, nonclinical testing using small sample sizes or short implant durations for *in vivo* animal studies may be sufficient to justify initiation of an early feasibility study. Under this approach, if additional and longer-term bench and animal testing are needed to support a larger clinical study of a near-final or final device design, these tests could be completed concurrently with the early feasibility study.

[25] See 21 CFR parts 50 and 56. [11]

21 CFR 812.27(a).

Some essential elements of a pivotal study, such as a prospective definition of study success and a prespecified data analysis plan, are not necessary for early feasibility study IDE applications. In addition, an early feasibility study protocol may be subject to fewer constraints as compared to a pivotal study protocol. For example, for early feasibility studies, sequential enrollment typically would not be necessary.

6. Report of Prior Investigations

The requirements in 21 CFR 812.27 apply to the Report of Prior Investigations for early feasibility study IDE applications. The information in this section is intended to clarify how certain of these requirements apply to early feasibility studies and to provide guidance on the content of the Report of Prior Investigations for an early feasibility study IDE.

The Report of Prior Investigations must include the information needed to justify a clinical investigation of a device.[11] For early feasibility studies, this information should:

- support an expectation of acceptable clinical use (e.g., successful device placement using a benchtop model that simulates clinical conditions and/or a suitable animal model) and that the device will function as intended;
- address basic device safety, including, but not limited to, sterility, biocompatibility, software verification and validation, electromagnetic compatibility, chemical compatibility (e.g., with concomitant drugs); and
- characterize catastrophic failure modes and identify risk mitigation approaches.

When adequately justified, the information may be generated from tests utilizing nonstandardized methodologies (e.g., using loading conditions that are not specified in a guidance document or voluntary standard to evaluate fatigue properties of a device for a new intended use, or using less sensitive testing equipment than specified in a standard). In determining the testing needed, the sponsor should consider the clinical significance of potential failures and the ability to predict clinical performance based on nonclinical testing. A sponsor may be able to justify deferral of certain testing until later stages of device development.

6.1 Content of the Report of Prior Investigations for an early feasibility study IDE

The information to be provided in the Report of Prior Investigations for an early feasibility study IDE application should be presented in three main sections: (1) Background, (2) Executive Summary, and (3) Detailed Reports:[26]

(1) The Background section should emphasize the unique aspects of the device design and intended patient population that will be considered when FDA evaluates whether the information provided justifies the initiation of an early feasibility study. This section should describe:

[26] Please consult 21 CFR 812.27 for the elements that must be included in a Report of Prior Investigations.

- the clinical context for the early feasibility study:
  - the clinical condition the device is intended to treat or assess;
  - the standard of care, including the types and severity of risks and the benefits associated with current treatment options;
  - the types and severity of potential risks and the anticipated benefits that may be associated with the study device; and
  - the rationale for exposing the target population to the potential risks (i.e., whether the anticipated benefits that may be associated with the use of the study device justify the potential risks, recognizing the benefits and risks posed by current treatment or assessment options);
- the design concept; and
- a summary justification regarding the amount and type of information/data needed to support initiation of the early feasibility study in the specified patient population, with comment on, or comparison to, what may be expected to support the initiation of a larger clinical study.

(2) The Executive Summary section should provide a summary of the information provided and an explanation as to why this information is adequate to support study initiation. This section should include:

· a summary description of the nonclinical testing that has been performed and relevant clinical information;

· a device evaluation strategy table, as described below, that references the relevant individual test reports for the data and/or information collected to address each device or procedure-related attribute; and

· a table describing the purpose of each test or analysis, test sample description, sample size, acceptance criteria (if available), test results, any potential clinical significance of the results, and cross reference to the test reports.

(3) The Detailed Reports section should include the reports for tests conducted and additional information available to support the initiation of the early feasibility study. This section should include:

· individual reports for each bench and laboratory test, computational modeling analysis (e.g., finite element analysis), and *in vivo* animal study:

  - each test report should include the purpose, test method, sample selection, results, discussion of the acceptability of the results, and when appropriate, justification and clinical applicability of the acceptance criteria;[27]

[27] Characterization tests (i.e., testing conducted to describe the device) may not have specified acceptance criteria and it may not be possible to establish acceptance criteria until clinical data are obtained.

· a summary of leveraged nonclinical information in appropriate detail, depending on the source of the information, such as:

- individual test reports not previously submitted to FDA;
- references to previously reviewed regulatory submissions;
- reports in the published literature

· a summary of any relevant clinical information, with references, if available.

The following sections provide further guidance on the purpose and preparation of the key elements of a Report of Prior Investigations for an early feasibility study IDE.

6.2 Design concept

The Background section of a Report of Prior Investigations for an early feasibility study IDE should include information to clearly describe the design concept, such as the:

· device description (e.g., physical description, figures, materials of construction, software documentation), principles of operation, what the device key design features are intended to do, and how the key design features accomplish the intended objective;

· intended clinical use, designated by the medical condition or lesion type to be treated or assessed, and any associated anatomical locations and limitations;

· conditions of use/intended *in vivo* environment; and

· minimum design-life of the device (i.e., the minimum duration for which a device has been designed to function as intended).

The device design concept provides the basis for identifying the appropriate testing and test methodologies and guides the device evaluation strategy.

6.3 Device evaluation strategy

The device evaluation strategy in the Executive Summary section of a Report of Prior Investigations should describe and justify the leveraged information and testing conducted to support initiation of an early feasibility study, with cross-references to the Detailed Reports section of a Report of Prior Investigations. The purpose of the device evaluation strategy is to facilitate FDA's understanding of the value of the leveraged information and why the information included in the Report of Prior Investigations is adequate to support IDE approval. To maximize the efficient use of sponsor and FDA resources, it is desirable for the sponsor to consult with FDA and for both parties to reach agreement on the strategy before the sponsor conducts the proposed testing. Therefore the device evaluation strategy would optimally be discussed during Pre-Sub interactions. This is particularly important when:

· the sponsor is providing less nonclinical data as compared to what would be expected for a traditional feasibility or pivotal study;

· there is no FDA guidance or voluntary standard specific to the device and intended use proposed to be studied; and/or

· certain nonclinical tests are more relevant than others in addressing basic safety and potential catastrophic failures, or to support basic device functionality.

Section 6.3.1 describes a systematic method for presenting the device evaluation strategy for an early feasibility study. This method involves identifying the key information necessary to justify initiation of the study based on a risk assessment, taking into consideration the anticipated benefits that may be associated with the device.

Even if testing has been done in accordance with a guidance document or voluntary standard, a justification should be provided to explain why the testing specified in the guidance or standard applies to the device and its intended use. This may involve a modification of the device evaluation strategy process described in Section 6.3.1, focusing on the unique aspects of the device or intended use as compared to those specifically addressed by the guidance or standard.

Section 6.3.2 presents an option for obtaining early FDA feedback on a comprehensive device evaluation strategy that extends beyond the early feasibility phase.

6.3.1 Device evaluation strategy for an early feasibility study

The device evaluation strategy for an early feasibility study should be based on a risk/benefit assessment.[28] In general, for an early feasibility study, the evaluation strategy should be focused on identifying the information needed to address significant safety concerns and support basic device functionality.

The device evaluation strategy is best outlined in a table, with the following column headings:

- *Column 1, Device Attribute*: Each procedure-related function, performance-related function, and basic safety-related feature required for the device to achieve the desired performance (i.e., benefit).

Note: For the purpose of the device evaluation strategy, a function is defined as the ability of the device to accomplish a goal and a feature is defined as an essential property of the device.

- *Column 2, Potential Failure Modes*: For each Device Attribute, the types of problems or failures that might occur and could result in consequences to the device or study subject if the function or feature is not attained.
- *Columns 3 and 4, Potential Device and Clinical Effects of Failure*: For each Potential Failure Mode, the potential effects of the failure mode on the device and/or study subject

(i.e., risks).

- *Column 5, Device Design Information*: For each Potential Failure Mode, the design characteristics intended to provide the function or feature or to address or mitigate the potential failure mode. Relevant anticipated benefits associated with the design characteristics may be highlighted in this column.

[28] At the early feasibility stage, a descriptive assessment may be more informative than a formal failure modes and effect analysis (FMEA), which provides a quantitative ranking of risks.

- *Columns 6 and 7, Leveraged Nonclinical Information and Supportive Clinical Information*: For each Attribute and/or Potential Failure Mode, the information from internal or external sources to supplement the assertions that:

    a) the function or feature will be attained; and/or
    b) the failure mode will not likely occur or will not be catastrophic if it does occur.

- *Column 8, Nonclinical Device Testing*: The bench, laboratory, analytical, and/or animal testing of the study device (i.e., the device that will be used in the clinical study) to complete the evaluation of the attribute and the potential failure mode(s).
- *Column 9, Clinical Study Mitigation Strategies*: For each Potential Clinical Effect of Failure, the mitigation strategies included in the clinical protocol intended to minimize the frequency or severity of the potential clinical effects resulting from a failure to attain the attribute.

Note: Although the Clinical Study Mitigation Strategies are a subset of the risk mitigation strategies included in the risk analysis section of the Investigational Plan, they should be presented within the device evaluation strategy table to emphasize their applicability to specific failure modes and effects of failure.

Table 1 defines the device evaluation strategy column headings and Table 2 describes the information recommended for inclusion in a device evaluation strategy table.

Table 1: Column Definitions for a Device Evaluation Strategy Table

Column 1	Column 2	Column 3	Column 4	Column 5	Column 6	Column 7	Column 8	Column 9
				Knowledge Base				
		Potential Effects of Failure			Supportive Information			
Device Attribute	**Potential Failure Modes**	**Potential Device Effects of Failure**	**Potential Clinical Effects of Failure**	**Device Design Information**	**Leveraged Nonclinical Information**	**Supportive Clinical Information**	**Nonclinical Device Testing**	**Clinical Study Mitigation Strategies**
Each individual device function or feature required for the device to achieve the overall desired performance. Note: A function is the ability of the device to accomplish a goal and a feature is an essential property of the device.	The failures that might occur and could result in consequences (effects) to the device or study subject if the function or feature is not attained.	The potential effect(s) of the failure mode on the device.	The potential effect(s) of the failure mode on the study subject.	The design characteristics intended to provide the function or feature or to address or mitigate the potential failure mode, and the anticipated benefits of these characteristics. And, if applicable, relevant information considered in the design of the device (i.e., design input) to support the assertions that: a) the function or feature will be attained; and/or b) the failure mode will not likely occur or will not be catastrophic if it does occur.	Nonclinical information leveraged from internal or external sources to support the assertions that: a) the function or feature will be attained; and/or b) the failure mode will not likely occur or will not be catastrophic if it does occur.	Relevant clinical experience obtained from internal or external sources for a similar device or indication to support the assertion that: a) the function or feature will be attained; and/or b) based on an evaluation of the clinical effects of failure, the failure mode will not likely occur or will not be catastrophic if it does occur.	Bench, laboratory, analytical, and/or animal testing of the study device (i.e., the device that will be used in the clinical study) to complete the evaluation of the attribute and the potential failure mode(s), considering the information in Columns 3-7 and 9.	Mitigation strategies included in the clinical protocol intended to minimize the frequency or severity of the potential clinical effects resulting from a failure to attain the attribute.

Table 2: Information To Be Included In The Device Evaluation Strategy Table

Column 1	Column 2	Column 3	Column 4	Column 5	Column 6	Column 7	Column 8	Column 9
				Knowledge Base				
Device Attribute	Potential Failure Modes	Potential Effects of Failure		Device Design Information	Supportive Information		Nonclinical Device Testing	Clinical Study Mitigation Strategies
		Potential Device Effects of Failure	Potential Clinical Effects of Failure		Leveraged Nonclinical Information	Supportive Clinical Information		
List each procedurerelated function needed for the device to be used successfully. List each performancerelated function or feature needed for acceptable device performance. List each necessary basic safety-related feature.	For each attribute, list the failure modes that could result if the attribute is not attained.	For each failure mode, list the potential effects of the failure mode on the device.	For each failure mode, list the potential effects of the failure mode on the study subject.	List the design characteristics intended to: a) provide the function or feature, identifying any anticipated benefits that may be associated with the characteristics; or b) address or mitigate the potential failure mode. And, if applicable, identify and reference the relevant information considered in the design of the device (i.e., design input) to support the assertions that: a) the function or feature will be attained; and/or b) the failure mode will not likely occur or will not be catastrophic if it does occur.	Identify and reference the nonclinical information leveraged from internal or external sources to support the assertions that: a) the function or feature will be attained; and/or b) the failure mode will not likely occur or will not be catastrophic if it does occur. Explain and justify how the specific aspects of the testing or analysis are relevant to the evaluation of the attribute or failure mode under consideration.	Identify and reference any relevant clinical experience obtained from internal or external sources for a similar device or indication to support the assertion that: a) the function or feature will be attained; and/or b) based on an evaluation of the clinical effects of failure, the failure mode will not likely occur or will not be catastrophic if it does occur. Explain and justify how the specific aspects of the clinical experience are relevant to the evaluation of the attribute or failure mode under consideration.	List and reference the testing and/or analyses on the study device (i.e., the device that will be used in the clinical study) to evaluate the attribute and the potential associated failure mode(s). For tests or analyses intended to address multiple attributes, identify the specific aspects of the testing or analysis relevant to the evaluation of the attribute or failure mode under consideration.	Identify any applicable mitigation strategies that will be utilized during the clinical study to minimize the frequency or severity of the potential clinical effects resulting from a failure to attain the attribute.

The process of constructing the device evaluation strategy table can be divided into four parts:

1) **Device Deconstruction** – identify the attributes needed for the device to achieve the design goals (Column 1), the potential failure modes (Column 2), and the effects of failure (Columns 3 and 4).

2) **Knowledge Base and Mitigation Strategies** – describe what is known from the device design (Column 5), leveraged nonclinical and clinical information from internal or external sources (Columns 6 and 7), and the clinical study mitigation strategies (Column 9) applicable to the attributes and failure modes.

3) **Evidence Gaps** – identify gaps in the existing information indicating that additional testing may be needed to justify study initiation, considering the Knowledge Base and focusing on the following:

   a. attributes most important for the intended use;
   b. potential failure modes most likely to be associated with catastrophic failures; and
   c. basic safety requirements (e.g., biocompatibility).

4) **Filling the Gaps** – identify in Column 8 the bench, laboratory, analytical, and/or animal testing to complete the evaluation of the device attributes and the potential associated failure modes, considering the following:

   a. Evidence Gaps;
   b. clinical context for the early feasibility study [see Section 6.1(1)];
   c. potential types, frequency, and severity of the clinical effects of failure that may be associated with the device or procedure; and

   d. Mitigation Strategies.

Any implications of the unique aspects of the device or the proposed intended use should be emphasized in the device evaluation strategy table. Similarly, the items listed under the Evidence Gaps (3a-c), above should be highlighted in the table.

Submitting the draft device evaluation strategy table in a Pre-Sub will maximize efficiency. In the draft table, the Nonclinical Device Testing (Column 8) may include proposed or completed testing, but reaching consensus with FDA on the appropriate testing prior to completion is preferable. Pre-Sub discussions on the device evaluation strategy table may focus on the following:

· whether Columns 1-4 (the Device Deconstruction) are complete,

· the applicability and usefulness of the information in Columns 5-7 and Column 9 (the Knowledge Base and Mitigation Strategies),

· whether the right information was considered when identifying the Evidence Gaps, and

· whether the additional proposed (or completed) testing described in Column 8 (Filling the Gaps) will likely complete the evaluation of the attribute or failure mode.

These discussions should continue under the early feasibility IDE, when the device evaluation strategy table has been further refined, and should focus on whether the information and data provided adequately address the specific attributes or failure modes.

For the early feasibility IDE, the level of detail to include in each row of the device evaluation strategy table should be proportional to the importance of the attribute to the intended use, the potential severity of the failure modes, and whether the method of assessing the attribute or failure mode is generally understood. A summary of Knowledge Base and Mitigation Strategies information should be included in the rows of the table for the most critical attributes for achieving the intended function of the device and for the potentially catastrophic failure modes. Descriptive information should be included for novel methods of assessment. Conversely, for less critical attributes, less clinically relevant failure modes, and standardized methodologies, it may be adequate to simply identify the applicable information or tests without providing descriptive information in the table. A comprehensive presentation of all leveraged information and completed testing should be included in the Detailed Reports section of the Report of Prior Investigations. Interaction between the sponsor and FDA is encouraged to establish consensus on the most important attributes and to determine the appropriate level of detail that should be included in the rows of the table.

It is understood that there may be uncertainty regarding some elements of the device evaluation strategy, depending on the novelty of the device or intended use. The device evaluation strategy table should be updated as new information emerges about the potential risks and the appropriate assessment of the device.

Depending on the device and intended use, it may be appropriate and acceptable to defer some device testing until after the early feasibility study, if the testing will not provide additional meaningful information regarding basic device safety or functionality. For some devices or intended uses, particularly for highly innovative devices, FDA recognizes that appropriate nonclinical test methodologies to assess some critical parameters may not be available or are impractical to complete, and therefore, these parameters would need to be evaluated clinically.

An example of a portion of a draft device evaluation strategy table for a hypothetical permanently implanted, percutaneously delivered, covered metallic device is presented in Appendix 2.

6.3.2 Overall device evaluation plan (at the sponsor's discretion)

It may be useful to obtain FDA feedback on the overall device evaluation plan. The plan would identify the types of information or levels of testing that may be needed to progress beyond an early feasibility study and propose the timing of deferred or additional testing.

The additional information/data that may be used to support progression to each of the planned developmental phases (e.g., traditional feasibility study, pivotal study, marketing application) can be listed in Column 8 (Nonclinical Device Testing) of the device evaluation strategy table. It should be noted that not all developmental phases may be necessary for every new device or intended use.

6.4 Bench and laboratory testing and computational modeling

For early feasibility studies, the full battery of tests that would be expected for evaluation of a final device design is not required for IDE approval. As outlined in Section 6.3 FDA encourages sponsors to consider the relationship between a device attribute or failure mode and the anticipated clinical consequences to determine the testing needed to support the IDE application. This approach may be used when justifying the device evaluation strategy, including the use of preliminary results or deferral of certain testing at the early feasibility phase of device development.

Computational modeling (CM) can be used for a variety of purposes to support the initiation of an early feasibility study. For example:

- For long-term implants in which the boundary and loading conditions are known, CM may be used to predict the long-term durability of the device.
- For long-term implants in which the boundary and loading conditions are not welldefined, CM may be useful for iterative design modifications, where simulations can be used to optimize the device design or enhance the design of prototypes.
- For certain test scenarios, which cannot be evaluated using other nonclinical methods or clinically, CM may be used. For example, to aid in assessing MRI safety, CM may be used to simulate certain worst-case MRI conditions that cannot be replicated in an animal model and cannot be tested ethically in humans.

Discussions with FDA regarding protocols for complex and novel testing are strongly encouraged.

6.5 In vivo animal studies

In vivo animal studies provide unique anatomic and clinical pathologic information on the local and systemic responses to device use. An animal study may be conducted to support the initiation of an early feasibility study when an animal model is needed to further assess basic safety or device functionality beyond the information provided from non-animal testing.

An animal study should involve the use of a validated animal model, when available, for which the results are likely to predict risks in humans. In cases in which a validated animal model is unavailable, a focused animal study to address a limited range of safety issues may be conducted to complement the non-animal testing. A rationale for addressing questions typically answered by animal studies with alternative methods or data should be provided in the IDE application.

Animal studies should not be viewed as an alternative to adequate bench testing, and whenever possible, protocols should apply the principles of reduce, replace, and refine. For example, substitutions for the use of live animals, such as *in vitro* methods (e.g., validated cell culture experiments), cadaveric studies, or the use of computer simulation may be considered. The size of the animal study depends on the device and how well the animal model provides anatomic, physiologic, and procedural similarities to humans. Recognizing the inherent variability of results, animal studies should be large enough to show consistent results. Short-term animal studies may be adequate for the initiation of an early feasibility study. However, additional

animal study data may be needed to support a larger clinical study with a near-final or final device design.

Good Laboratory Practices (GLP) for animal care and study conduct as specified in 21 CFR part 58 assure the quality and integrity of safety data to support IDE applications. Non-GLP study data may be used to support an early feasibility study IDE application only if the deviations from GLP are identified and justified and do not compromise the validity of the study results.[29] For example, if an independent quality assurance unit is not utilized, a sponsor should describe how bias was mitigated and how the study was verified to be authentic and complete. Both GLP and non-GLP studies should include independent monitoring and assessments with full disclosure of study findings.

Discussions with FDA on study protocols, including the evaluation of operator technique, safety outcomes, and the effects of the biological system on the device, are encouraged prior to the initiation of *in vivo* animal studies.

6.6 Prior clinical information

For all IDEs, a summary of any prior clinical studies of the device used for the proposed intended use must be provided in the Report of Prior Investigations.[16] For early feasibility studies, although clinical data may not be available for the test device for its proposed intended use, any relevant background clinical information should also be provided. Relevant information includes data or publications on:

- similar or related devices utilized for the proposed intended use; or
- the subject device or similar devices used for a different purpose. This information may come from clinical use outside of the United States and may be used to support proof of principle and/or to address the likelihood of potential failure modes that may be observed during the early feasibility study. If such information is available, it should be summarized in a format appropriate for the type of information (e.g., clinical study reports, summaries of publications with copies of the citations, individual experience with the device or prototype outside of a clinical study).

7. Investigational Plan

The requirements in 21 CFR 812.25 apply to the Investigational Plan for early feasibility study IDE applications. The information in this section is intended to clarify how certain of these requirements apply to early feasibility studies. In the IDE application, the study should be clearly designated as an early feasibility study. The proposed study should reflect the novelty of the device and medical need. Use of the Pre-Sub process to discuss the Investigational Plan with FDA is highly recommended.

Note that small clinical trials to determine device feasibility are specifically excluded from the definition of "applicable device clinical trials" requiring registration on www.ClinicalTrials.gov. 17 FDA is interpreting this exception to apply to early feasibility studies.

[29] See 21 CFR 812.27(b)(3).

7.1 Risk analysis and mitigation

The Investigational Plan must include a thorough risk analysis which describes the type and estimated severity of risks to the subjects, how risks will be minimized, and a justification that the risks are reasonable in relation to the expected benefits.[18] The risk analysis should include the anticipated benefits and potential clinical effects of failure identified in the device evaluation strategy, as well as risks independent of the device that may be related to the underlying disease comorbidities, or inherent to the procedure, and benefits unique to the device concept. For example, a risk analysis may include the risks associated with use of anesthetic and contrast agents and the benefits of a less invasive intervention.

For an early feasibility study, the methods to minimize risks may include the use of standard approaches, with additional mitigation strategies to protect individual study subjects and future study participants during the ongoing early feasibility study. Examples of both standard and additional risk mitigation strategies include:

- use of study sites that have sufficient expertise and resources to manage adverse events and provide appropriate alternative therapies if needed;
- identification of qualified investigators with adequate training to conduct the early feasibility study;
- a plan to capture human factors information during the course of the study to modify the procedures or device as necessary based on the information obtained;
- specifying appropriate study inclusion and exclusion criteria;
- limiting the sample size to a reasonable number for an early feasibility study (e.g., 5-10 initial subjects);
- follow-up assessments at regular intervals to monitor subject safety and device effectiveness (i.e., potentially more frequent than for a traditional feasibility or pivotal study);
- timely reporting of serious adverse events (e.g., after each occurrence rather than only in a periodic progress report);
- timely reporting of device performance parameters, which help determine whether the device functions as intended (e.g., measurements of deliverability, stability, handling, visualization, patency, integrity);
- non-sequential enrollment, that is, initial device use in subjects with more favorable anatomical characteristics as compared to the population otherwise eligible for the early feasibility study (e.g., selecting subjects that meet study eligibility requirements but do not have anatomic features that may increase the difficulty of device use); and
- a pre-specified plan for periodic patient outcome assessments and reporting prior to enrollment of additional patients (e.g., as frequently as after each use of the device).

7.2 Clinical protocol

The Investigational Plan for an early feasibility study must present objectives that reflect the purpose of the clinical study.[19] The study protocol should include study endpoints, endpoint assessment methods, and adverse event definitions as appropriate for an early feasibility study. The study protocol must also clearly describe the methodology to be used in the investigation.[20]

This should include a comprehensive description of the subjects to be enrolled in the study. When identifying the appropriate study population, subject risk tolerance (based on the severity of the underlying condition and limitations of alternative treatment options) and the ability to utilize the standard of care if the study device does not function as intended should be considered. The subjects may have different clinical characteristics as compared to the population to be included in a future pivotal study (e.g., the early feasibility cohort may have more comorbidities, or a more advanced stage of disease). However, to ensure that the study

[19] 21 CFR 812.25(a).

[20] 21 CFR 812.25(b).

will provide information useful for the device development process, and to avoid exposing subjects to risks in the absence of any anticipated benefit, the study should avoid enrolling subjects for whom success is unlikely due to general health issues.

To allow for appropriate flexibility with respect to patient selection and data interpretation, the early feasibility study protocol generally does not need to include the same level of detail as a pivotal study protocol (see Section 5), but it needs to ensure adequate capture of adverse clinical events and device performance information.

7.3 Human subject protection measures

Any early feasibility study involving human subjects must comply with FDA human subject protection requirements, including obtaining informed consent and Institutional Review Board (IRB) (or ethics committee) oversight.[30] These measures should be tailored to the subject population and the risk profile of the device under investigation.

7.3.1 Informed consent

Sponsors, investigators, and IRBs should pay particular attention to the adequacy of informed consent in early feasibility studies. The informed consent process for early feasibility studies, as for all clinical investigations, must adhere to the requirements described in 21 CFR part 50 subpart B – Informed Consent of Human Subjects. An informed consent form for early feasibility studies must comply with the requirements in 21 CFR 50.25 and should address the distinctive aspects of an early feasibility study. For example, subjects must be told that the study involves research and must be provided an explanation of the purposes of the research,[22] including that the proposed investigation is an early feasibility study (e.g., a small study of an innovative device or innovative clinical use of a device for which there may be less nonclinical data than would be required for a larger study). The novelty of the device or procedure must also be described in language understandable to the subject.[23]

As discussed above, an early feasibility study may carry greater unknown risk as compared to traditional feasibility and pivotal studies. Subjects must be made aware during the informed consent process that there may be unforeseeable risks associated with participation in the study due to limitations in available data and experience with the device.[24] A description of any benefits to the subject or to others which may reasonably be expected from the research must be

[30] See 21 CFR parts 50 and 56.

provided during the informed consent process in accordance with 21 CFR 50.25(a)(3). For example, the form should note that even if there is limited or no expected personal benefit to the study subject, future patients with the disease or condition may benefit from the information obtained during the early feasibility study. The consent form should not include language that could lead subjects to overestimate the chance of personal benefit.

Additional guidance on the information to include in an informed consent form for an early feasibility study can be found in Appendix 3.

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7.3.2 Institutional Review Boards

As with all clinical investigations, early feasibility studies must adhere to the requirements for study oversight by an IRB, as described under 21 CFR part 56. For example, IRBs must determine if the risks to the subjects are minimized to the extent possible, and consider whether the risks to the subjects are reasonable in relation to anticipated benefits and the importance of the knowledge that may be obtained.[25]

IRBs must conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year, as required by 21 CFR 56.109(f). It is likely that more frequent oversight by the IRB to assure human subject protection may be appropriate for early feasibility studies. This may include, for example, continuing review on a more frequent basis than annually, continuing review after a small target number of subjects have been studied, and/or graduated enrollment based upon a safety analysis of the preceding subjects.

7.4 Monitoring

7.4.1 Monitoring procedures

Detailed monitoring procedures, appropriate for an early feasibility study, must be included in the Investigational Plan, as required by 21 CFR 812.25(e). For more information on standard monitoring procedures, see FDA's draft guidance, "Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring" (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269919.pdf). FDA's draft guidance represents FDA's proposed approach on this topic. Due to the limited number of study sites and subjects, and the expected close oversight of each study subject, the monitoring procedures for early feasibility studies may deviate from standard procedures and should be tailored to the particular study being conducted.

7.4.2 Data monitoring committee (DMC)

FDA's guidance, "Establishment and Operation of Clinical Trial Data Monitoring Committees," (http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127073.pdf) notes that:

> [E]arly studies are often exploratory in nature; they are frequently not randomized or controlled and therefore accumulating results are known to the investigators and sponsor. Issues regarding statistical interpretation of interim data, or confidentiality of interim data, are therefore generally less relevant in this setting. Nevertheless, for difficult

situations in which the potential scientific gain from continuing a study must be evaluated in the context of ethical considerations for ensuring subjects' rights and welfare, particularly in settings such as those described above, DMCs may be helpful to investigators, sponsors, and IRBs by providing independent, objective expert counsel.

For certain early feasibility studies, a DMC composed of clinicians, scientific experts, and individuals with ethical expertise may be helpful in evaluating data relatively early in the course of the study and would provide an additional layer of human subject protection. Use of a DMC could be proposed by a sponsor as a risk mitigation strategy element, particularly for studies where additional independent oversight would be of value.

8. Iterations during early feasibility studies

Because modifications to the Investigational Plan are expected during early feasibility studies, discussions with FDA to facilitate timely implementation of changes are particularly important throughout the Pre-Sub and IDE processes. The requirements outlined in 21 CFR 812.35 and explained in, "Changes or Modifications During the Conduct of a Clinical Investigation; Final Guidance for Industry and CDRH Staff" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm082145.htm), regarding changes to a device or clinical protocol apply to all types of investigational studies. However, this guidance describes new policy, interpreting the requirements differently for early feasibility studies.

To facilitate timely device and/or clinical protocol modifications during an early feasibility study, this guidance introduces the following approaches:

1. Permitting a broader array of modifications to the device and the clinical protocol under 5-day notification without prior FDA approval during an early feasibility study as compared to other types of studies;

2. For anticipated changes that would require prior FDA approval, allowing a sponsor to seek **contingent approval** beforehand, which would permit changes contingent upon acceptable nonclinical test results without requiring additional FDA action;

3. For early feasibility study IDE supplements and amendments, utilizing a new **interactive review** process that encourages communication with FDA during the 30-day review cycle.

Note that annual progress reports to the FDA are required by 21 CFR 812.150(b)(5) for studies of significant risk devices. Some minor changes to the purpose of the study, risk analysis, monitoring procedures, labeling, informed consent materials, and IRB information are not

required to be submitted in supplemental applications but must be identified in these annual progress reports. [31]

8.1 Changes requiring FDA notification (5-day notice)

For all IDEs, a sponsor may make certain changes to an investigational device or clinical protocol during the study without prior FDA approval of a supplemental application by submitting a notice to FDA within 5 working days of making the change.[27] A sponsor may make changes with 5-day notice if: (i) the changes to the device are made in response to information gathered during the course of the investigation, and the changes do not constitute a significant modification in design or basic principles of operation; or (ii) the changes to the clinical protocol do not affect: (a) the validity of the data or information, or the relationship of likely patient risk to benefit relied upon to approve the protocol, (b) the scientific soundness of the plan, or (c) the rights, safety, or welfare of the human subjects involved in the investigation.[28] The information to be included in such a notice is described in 21 CFR 812.35(a)(3)(iv).

Device developmental changes that do not constitute a significant change in design or basic principles of operation are generally appropriate for 5-day notices. For early feasibility studies, FDA would consider a broader range of changes not to be significant as compared to other types of studies. This is in part because the evaluation of an early feasibility study does not depend on statistical analyses of data collected or the pooling of data among study subjects, which would require the use of a consistent device design. However, the changes should be expected not to adversely affect device performance or pose additional risk to the study subjects.

For changes to an early feasibility study clinical protocol, the most relevant requirements for application of the 5-day notification option are that the changes: (1) not alter the relationship of likely subject benefit and risk relied upon to approve the protocol, and (2) not affect the rights, safety or welfare of study subjects.[29] Since, as discussed above, early feasibility studies are expected to have enhanced risk mitigation strategies and patient protection measures directed toward each study subject, sponsors should explain how these instruments provide additional support when considering changes appropriate for implementation under a 5-day notice. The other criteria, specifically that changes to the clinical protocol not affect the validity of the data or the scientific soundness of the investigational plan,[30] should generally be much easier to meet for early feasibility studies than for other studies, because these studies are not intended to obtain statistically valid data or test statistical hypotheses.

The types of changes that may be considered for 5-day notices may be discussed during Pre-Sub interactions and prospectively identified within the IDE application to facilitate timely implementation of device and clinical protocol modifications. For changes that are appropriate for implementation under a 5-day notice, the contingent approval process (described below), in which the information needed to justify a change is identified, may be used as an alternative approach.

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[31] See 21 CFR 812.35(a)(4).

[27] 21 CFR 812.35(a)(3).

Appendix 4 includes examples of the types of changes that may be appropriate for 5-day notification during an early feasibility study.

8.2 Changes requiring FDA approval

The first step in obtaining FDA approval of changes during the early feasibility study should be informal discussion with FDA, using the Pre-Sub process when appropriate, to identify the proposed modifications, the reasons for the modifications (e.g., adverse events observed during the clinical study), the purpose of the modifications, and the evaluations needed to support use of a modified device and/or changes to the clinical protocol.

Following the informal discussion, there are two new approaches for obtaining timely FDA approval of changes to early feasibility studies: 1) contingent approval and 2) interactive review.

[28] 21 CFR 812.35(a)(3)(i) and (ii). These changes must be supported by credible information as defined at 21 CFR 812.35(a)(3)(iii). 21 CFR 812.35(a)(3).

[29] See 21 CFR 812.35(a)(3)(ii).

[30] 21 CFR 812.35(a)(3)(ii)(A) and (B).

1) Contingent approval. When device iterations or changes to the clinical protocols are anticipated, identified, and explained prospectively, the contingent approval process may be used. This process may be informally discussed during Pre-Sub interactions and formally proposed during the original early feasibility study IDE application or in IDE supplements.

In order to obtain contingent approval, during the 30 day review cycle the sponsor and FDA should reach final concurrence on the nonclinical test plan and associated acceptance criteria to evaluate the anticipated changes. Once these are agreed upon, FDA may approve the anticipated changes contingent on the sponsor's successful completion of the test plan and the reporting of the test data to FDA within 10 calendar days of implementing the change.

If the sponsor deviates from the conditions of FDA's approval, the contingent approval would no longer be valid, and the sponsor would need to renegotiate the test plan with FDA and obtain a new contingent approval. Alternatively the sponsor could seek approval through the submission of a 30-day IDE supplement.

If the sponsor is able to anticipate multiple changes to the clinical protocol or potential device iterations, a proposal that covers these changes may be provided in the original early feasibility IDE application or in a single supplement. For device modifications, the sponsor would need to prospectively identify the appropriate testing plan and acceptance criteria for each type of change to allow for contingent approval of all of the proposed changes. For example, if a sponsor anticipates iterations of the materials of construction based on clinical data generated during the early feasibility study, they may present their strategy in a single IDE supplement and receive approval for the iterative plan, contingent on successful completion of the test plan for each material type. Within 10 days of implementing each change, an IDE supplement should be submitted to provide the data and to report to FDA the current device iteration being used in the study.

For the clinical protocol, the sponsor could propose changing several clinical parameters during the early feasibility study to determine the most relevant parameters for future evaluation of the device. If the sponsor can adequately justify the use of each parameter within the initial IDE submission or in an IDE supplement, the approval of the changes would be contingent only on reporting to FDA, within 10 days of implementing each change, that the changes were made. This report should include a copy of the clinical protocol currently being used. For other changes to the clinical protocol, it may be necessary to collect additional information (e.g., outcomes for the initial patients treated) to support the changes. In this case, FDA concurrence with the information to be collected and the results needed to support the change would need to be obtained prior to FDA granting contingent approval. The approval would be contingent on reporting the information, in addition to providing a copy of the protocol currently being used.

Appendix 4 includes examples of the types of changes that may be appropriate for contingent approval during an early feasibility study.

2) Interactive review. Interactive review involves the continuation of informal discussions with FDA during the 30-day IDE supplement review cycle. This process may be used in situations where the sponsor has completed nonclinical testing to evaluate device modifications, or where changes to the clinical protocol do not meet the criteria for a 5day notice, and FDA decides that the additional information needed to address outstanding questions can be provided and reviewed within the 30-day review cycle.

For this process, the sponsor should submit an IDE supplement that requests the modifications and addresses any prior FDA feedback. During the interactive review, FDA may request, and the sponsor may provide, additional information to enable the approval of the supplement within 30 days. The success of the interactive review process depends on the availability of FDA and sponsor resources to provide timely and high quality feedback, as well as the acceptability of the test results.

9. Design controls

The current good manufacturing practice requirements of the quality system regulation (21 CFR part 820) govern the methods used in, and the facilities and controls used for, the design, manufacture, packaging, labeling, storage, installation, and servicing of all finished devices intended for human use. An approved IDE exempts a device from the good manufacturing practice requirements under section 520(f) of the FD&C Act except for the requirements found in 21 CFR 820.30 (design controls).[31]

When complying with the requirements of 21 CFR 820.30 under an IDE, a device manufacturer shall establish and maintain a plan that describes or references the design and development activities specific to the medical device being designed or manufactured. This plan does not need to be submitted in the IDE application. The design plan shall describe or reference the following design and development activities in accordance with 21 CFR 820.30.

- Definition of responsibility for the implementation of the design and developmental activities;
- Identification and description of the interfaces with different groups or activities that provide or result in input to the design development process;
- Verification that the design outputs that are essential for the proper functioning of the device were identified;
- Formulation of a plan to conduct design reviews to assess the progress of the design, and confirm the design is ready to move to the next phase of development;
- Assurance that the design outputs met the design input requirements as part of the design verification;
- Completion of a design validation to show that the approved design met the predetermined user needs and intended uses;

- Performance of a risk analysis and consideration of risk throughout the design process;
- Documentation and control of design changes occurring during pre-production and post-production of the device; and
- Documentation of the design transfer into production specifications.

Appropriate documentation and establishment of the aforementioned elements of the device design plan will facilitate meeting the design control requirements in 21 CFR 820.30 as the device design evolves.

10. Next steps in clinical evaluation

After obtaining clinical information from an early feasibility study, the type of subsequent clinical evaluation will depend on whether changes in the device design are expected, the availability of adequate data to justify the next study, and the purpose of the clinical study. Early feasibility studies involve the investigation of devices that may be in a rapid phase of device iteration. If clinical information is needed after device modification and further device iterations are expected, a sponsor may submit an IDE supplement including a request for expansion of the early feasibility study. Once approved, the sponsor may enroll additional subjects in the early feasibility study. If the device design is near-final or final, and the results of the early feasibility study support the initial safety of the device and proof of principle, it may be more appropriate for the sponsor to pursue either a traditional feasibility study or a pivotal study. Progression to a traditional feasibility or pivotal study should be requested under an IDE supplement and should include the information needed to justify initiation of the larger study. The approval of any IDE supplement will ultimately depend on the availability of nonclinical and clinical data to justify initiation of the specific type of study requested.

Informal communications with FDA are important to help determine the most appropriate next step in the clinical evaluation of a device.

11. Conclusion

Early feasibility studies may be used to provide proof of principle and initial clinical safety data. Data from an early feasibility study may lead to device modifications and be used to refine the bench, analytical, and *in vivo* animal studies and future clinical study protocols.

Conducting an early feasibility study under an IDE provides a unique opportunity to obtain clinical experience with a new or modified device or new clinical use, while utilizing appropriate subject protection measures and good clinical study practices. Vital clinical information can be captured and used to optimize the device design, design evaluation, and clinical investigation plans.

Initiation of an early feasibility study and progression toward a pivotal study benefit from a flexible process that relies on sound nonclinical assessments and appropriate risk-based rationales. A high degree of interaction between FDA and the sponsor and use of the Pre-Sub process will be instrumental in the successful implementation of this guidance.

Appendix 1: Suggested topics for a Pre-Sub for an early feasibility study IDE

Although use of the Pre-Sub process is not a requirement, interactions between the FDA and sponsor are encouraged to enhance the predictability of the early feasibility study IDE review process. Based on the recommendations outlined in the guidance, the following topics may be useful to discuss during Pre-Sub interactions prior to the submission of the original IDE application:

1. Design concept

2. Clinical context
   a. Clinical condition the device is intended to treat or assess
   b. The standard of care, including the types and severity of risks and the benefits associated with current treatment options
   c. The types and severity of potential risks and the anticipated benefits that may be associated with the study device
   d. The rationale for exposing the target population to the potential risks (i.e., whether the anticipated benefits that may be associated with the use of the study device justify the potential risks, recognizing the benefits and risks posed by current treatment or assessment options)

3. Rationale for early feasibility study, considering:
   a. Novelty of the device or its intended clinical use
   b. Stability of the device design
   c. Whether additional nonclinical testing would likely provide the information needed to further device development

4. Nonclinical testing plan
   a. Draft device evaluation strategy for the early feasibility study
   b. Draft device evaluation strategy for device development beyond the early feasibility phase, if the sponsor wishes to obtain FDA feedback that may assist with future submissions
   c. Summary justification regarding the amount and type of information/data needed to support initiation of the early feasibility study in the specified patient population, with comment on, or comparison to, what may be expected to support the initiation of a larger clinical study
   d. Protocols for complex and novel nonclinical (e.g., bench, animal and computational modeling) testing or analyses, when available

5. Investigational plan
   a. Clinical study protocol summary
   b. Summary of risk analysis and mitigation strategies
   c. Informed consent language regarding the early feasibility nature of the study

6. Anticipated design iterations and clinical protocol changes and proposals for using the strategies outlined in the guidance

7. Projected device development timeline (e.g., significant regulatory and testing milestones)

Appendix 2: Device evaluation strategy example

The following hypothetical example illustrates the concepts described in Section 6.3.

A sponsor approaches FDA with an early feasibility study proposal to evaluate an innovative, covered, metallic implant to treat a disease common in the elderly. The device is unique in that delivery of the treatment will be through a catheter, rather than by open surgery (the standard of care). The expected benefits of this approach include less bleeding, fewer major adverse events, less pain, shorter hospital stay, and faster recovery as compared to the open surgery. There are aspects of the new device that are similar to a device approved for a different indication.

In a Pre-Sub, the sponsor describes the design concept and provides a draft device evaluation strategy table as described in Tables 1 and 2 of Section 6.3. Portions of the table are presented in Tables 3-5 for a procedure-related function, a performance-related function, and a basic safetyrelated feature.

The procedure-related functions for this device include the ability to: • access the target site;

- deploy the implantable portion of the device; and • withdraw the delivery system.

For the 'the ability to access the target site' attribute, the potential failure modes are: • the inability to safely advance the system to the target site; and • implant dislodgement from the delivery system.

Table 3 outlines the information for the attribute 'the ability to access the target site' and the potential failure mode of 'the inability to safely advance the system to the target site.'

Some of the performance-related functions and features include:

- implant integrity; • fixation effectiveness; and • patency.

For the 'implant integrity' attribute, the potential failure modes are:

- corrosion; and
- structural failure of the implant.

Table 4 outlines the information for the attribute 'implant integrity' and the potential failure mode of 'corrosion.'

The basic safety-related features include:

- biocompatibility; • sterility; and
- MR compatibility.

For the 'biocompatibility' attribute, the potential failure mode is 'non-biocompatibility.' Table 5 outlines the information for the attribute 'biocompatibility' and the potential failure mode of 'non-biocompatibility.'

Table 3: Device Evaluation Strategy Table, Procedure-Related Function – Ability to Access

Column 1	Column 2	Column 3	Column 4	Column 5	Column 6	Column 7	Column 8	Column 9
		Potential Effects of Failure			**Supportive Information**			
DeviceRelated Attribute	**Potential Failure Modes**	**Potential Device Effects of Failure**	**Potential Clinical Effects of Failure**	**Device Design Information**	**Leveraged Nonclinical Information**	**Supportive Clinical Information**	**Nonclinical Device Testing**	**Clinical Study Mitigation Strategies**
Device function or feature required for the device to achieve the overall desired performance	*The failures that might occur and could result in consequences (effects) to the device or study subject, if the function or feature is not attained*	*The potential effect(s) of the failure mode on the device*	*The potential effect(s) of the failure mode on the study subject*	*Relevant design characteristics intended to provide the function or feature or to address or mitigate the potential failure mode, and other information considered in the design of the device*	*Nonclinical information leveraged from internal or external sources*	*Relevant clinical experience obtained from internal or external sources for a similar device or indication*	*Proposed testing of the study device (i.e., the device that will be used in the clinical study) to complete the evaluation of the attribute and the potential failure mode(s), considering the information in Columns 3-7*	*Mitigation strategies included in the clinical protocol intended to minimize the frequency or severity of the potential clinical effects resulting from a failure to attain the attribute*

Ability to access the implantation site	Inability to safely advance the system to the target site	- Delivery system damage - Implant damage	- Embolism - Procedural failure - Tissue damage at access site	Design characteristics: - Unique tip to minimize tissue trauma - Enhanced flexibility to accommodate tortuous anatomy - Safety features to prevent completion of deployment steps out of sequence Relevant information considered in the design of the device: - Use of same delivery mechanism as our similar device with a known clinical performance (without catastrophic failures), approved to treat a different disease process in the same anatomic location	- Volume 2, Section 1 of the Pre-Sub describes nonclinical testing conducted on our similar device Reference to this information is appropriate because the study device has the same delivery mechanism as the approved, similar device.	- Volume 2, Section 2 of the Pre-Sub describes the clinical use of our similar device Reference to this information is appropriate because the new intended use does not involve targeting a new anatomical implantation site and therefore would not likely negatively affect the ability of the study device to access the implantation site.	The following tests will be conducted on the study device: - Acute and 30-day animal study (see study protocol in Volume 3, Section 1) - Simulated use testing (see protocol in Volume 3, Section 2) - Tensile bond strength - Torsional bond strength	For all events - Timely detection, treatment, and reporting of adverse events For 'Embolism' - Clinical evaluations and imaging post-procedure for early detection of distal organ damage to allow for early treatment and to identify the need to change the procedure or device - Embolic protection device use For 'Procedural failure' - Pre-operative imaging to confirm appropriate anatomy - Plan to treat subjects with the current standard of care if the delivery system cannot be advanced For 'Tissue damage at access site' - Pre-operative imaging to confirm appropriate anatomy

Table 4: Device Evaluation Strategy Table, Performance-Related Function – Implant Integrity

Column 1	Column 2	Column 3	Column 4	Column 5	Column 6	Column 7	Column 8	Column 9
		Potential Effects of Failure			Supportive Information			
DeviceRelated Attribute	**Potential Failure Modes**	**Potential Device Effects of Failure**	**Potential Clinical Effects of Failure**	**Device Design Information**	**Leveraged Nonclinical Information**	**Supportive Clinical Information**	**Nonclinical Device Testing**	**Clinical Study Mitigation Strategies**
Implant integrity	Corrosion	- Component separation - Fracture - Movement from intended implant location	- Foreign body embolization - Loss of biocompatibility - Effectiveness failure (specify) due to component separation - Effectiveness failure (specify) due to implant movement - Trauma to adjacent structures	Design characteristics: - Electropolished metallic components to improve corrosion resistance Relevant information considered in the design of the device: - Use of same metallic components and surface finishing as our similar, approved device with acceptable corrosion resistance	- Volume 2, Section 3 of the Pre-Sub describes nonclinical testing conducted on our similar device with known corrosion resistance Reference to this information is appropriate because the risk of corrosion is similar to the previously approved device. The study device will be exposed to an *in vivo* environment that has the same relevant characteristics (e.g., body fluid contact, externally applied forces), has a similar design and is constructed with the same metal, using the same manufacturing methods.	- Volume 2, Section 4 of the Pre-Sub describes the clinical use of our approved device Reference to this information is appropriate because the new device will be exposed to the same *in vivo* environment.	No devicespecific testing needed prior to initiation of the early feasibility study	For all events - Timely detection, treatment, and reporting of adverse events For 'Foreign body embolization, trauma to adjacent structures and all other clinical effects of failure' - No additional mitigation strategies beyond timely detection, treatment, and reporting of adverse events - For 'Loss of biocompatibility' - Assess inflammatory biomarkers post-procedure - Monitoring of subjects for signs and symptoms of allergic reactions to allow for early treatment

								For ‘Effectiveness failure (specify) due to implant movement or component separation’ - Imaging studies at regular intervals to evaluate device position - Plan to implant additional devices if the original device moves from the targeted implant site

Table 5: Device Evaluation Strategy Table, Basic Safety-Related Feature – Biocompatibility

Column 1	Column 2	Column 3	Column 4	Column 5	Column 6	Column 7	Column 8	Column 9
Device-Related Attribute		**Potential Effects of Failure**			**Supportive Information**			
	Potential Failure Modes	**Potential Device Effects of Failure**	**Potential Clinical Effects of Failure**	**Device Design Information**	**Leveraged Nonclinical Information**	**Supportive Clinical Information**	**Nonclinical Device Testing**	**Clinical Study Mitigation Strategies**
Biocompatibility	Non-biocompatibility	No device effects	Adverse biological response	Relevant information considered in the design of the device: - Use of materials with histories of clinical use	No leveraged nonclinical information Although the metallic component is identical to one of our approved devices, there are additional materials used in the construction of the device, and therefore, biocompatibility testing on the study device is needed.	No leveraged clinical information	The following tests will be conducted to support the initiation of the early feasibility study: - Testing in accordance with Part 1 of ISO 10993 (see Volume 3, Section 3) - Acute and 30-day animal study (see study protocol in Volume 3, Section 4) The specific aspects of biocompatibility that will be assessed in the animal study are acute systemic and subchronic toxicity, *in vivo* thrombogenicity, hemolysis and local irritation. These will be assessed through complete necropsy and target tissue gross and histologic evaluation.	For all events - Timely detection, treatment, and reporting of adverse events - For 'Adverse biological response or loss of biocompatibility' - Assess inflammatory biomarkers postprocedure - Monitoring of subjects for signs and symptoms of allergic reactions to allow for early treatment

To help support the device evaluation strategy, the sponsor identifies the novel and most clinically relevant attributes (i.e., those that support an expectation of acceptable clinical use or are associated with basic device safety) and those that could be affected by differences in their study device as compared to existing devices. The sponsor explains why certain potential failure modes would not likely be associated with catastrophic failures, discusses the likelihood and severity of the potential clinical effects of failure, emphasizes the unique anticipated benefits of their novel technology, and details how the mitigation strategies can be used to minimize harm to study subjects. The sponsor also describes their rationale for deferring some nonclinical testing.

The FDA interacts with the sponsor to reach agreement on the comprehensive list of devicerelated attributes and the potential failure modes that could occur if the desired functions or features are not achieved. They then discuss whether the proposed bench, laboratory, analytical, and animal testing of the study device should be adequate to complete the evaluation of the attributes and the potential failure modes, considering the information provided in Columns 5-7 of the device evaluation strategy table.

The sponsor plans to modify the device design based on the information obtained from the early feasibility study. The sponsor elaborates on the planned testing to be completed for the modified device, prior to progressing beyond the early feasibility study. For example, to justify the initiation of the early feasibility study, an animal study is planned to evaluate the potential for catastrophic failure of the device acutely and in the intermediate-term. To support initiation of a pivotal trial, the sponsor proposes a long-term animal study, which will be carried out concurrently with the traditional feasibility study, to demonstrate complete healing at the implant site. The sponsor will update their overall device evaluation strategy table as information is obtained from their nonclinical testing and early feasibility study.

The sponsor continues to interact with the FDA as they complete the nonclinical testing of their device. The Pre-Sub interactions regarding the device evaluation strategy enhance the predictability of the review process by increasing the likelihood that the Report of Prior Investigations will be adequate to help support IDE approval.

Appendix 3: Supplemental guidance for the preparation of an early feasibility study informed consent document

The informed consent process for early feasibility studies, as for all clinical investigations, must adhere to the requirements described in 21 CFR part 50 subpart B – Informed Consent of Human Subjects. The outline below presents the general informed consent requirements listed in 21 CFR 50.25. The specific recommendations relevant to an early feasibility study are found under each applicable general consent requirement. Some of these recommendations may be appropriate for other types of clinical studies, but are particularly relevant for early feasibility studies.

Note that the recommendations below are not presented in plain language. When drafting an informed consent form, appropriate wording should be used to effectively communicate the information to the potential study subject.

Introduction
General consent requirement: __ a statement that the study involves research

Early feasibility consent recommendations:
include a statement that this is an early feasibility study and explain the significance of such studies
describe the consent process and the purpose of the consent process
Note: It may be appropriate to have a patient advocate present during the consent process and/or have an independent individual, other than the investigator, be responsible for explaining the study.

Purpose of the Study General consent requirement: __ an explanation of the purposes of the research

Early feasibility consent recommendations:

Generic early feasibility study information describe an early feasibility study, that is, a study of an innovative device or innovative clinical use of a device in a small number of patients
explain that the study is designed to gain initial insights into the basic safety and device functionality
explain that there may be unforeseeable risks associated with participation in an early feasibility study due to limitations in available data and experience with the device

Specific information regarding the proposed investigation name the device and the number of patients to be enrolled
provide a brief description of the underlying medical condition, the device (including the innovative device features) and what the device is intended to do
explain how different the device or procedure is from currently available therapies provide information on whether this study involves the first human use of the device or whether there has been previous clinical use of this or a similar device for the same or a different intended use

Study Procedures General consent requirement: a description of the procedures to be followed

Early feasibility consent recommendation:
include a description of all procedures and follow-up requirements

General consent requirements: __ identification of any procedures which are experimental __ the expected duration of the subject's participation

Early feasibility consent recommendation:
indicate how the procedures and follow-up in the study differ from the standard of care

Risks
General consent requirement: __ a description of any reasonably foreseeable risks or discomforts to the subject

Early feasibility consent recommendations:
Note: This section should reflect the risk analysis and risk mitigation strategies in the clinical protocol.
include a statement to indicate that not all risks associated with the use of the study device are currently known
list reasonably foreseeable risks, but indicate that there may not be information to fully predict the frequency and severity of these risks
describe risk mitigation strategies (e.g., if the investigational treatment is unsuccessful, the patient may still be eligible for treatment with the current standard of care)

Benefits
General consent requirement: __ a description of any anticipated benefits to the subject or others

Early feasibility consent recommendations:
without overestimating the chance of personal benefit, describe any anticipated benefits to the subject which may reasonably be expected
disclose that there may be little information to support a likelihood of personal benefit indicate that even if there is limited or no personal benefit to the study subject, future patients with the disease or condition may benefit from the information obtained during the early feasibility study

Alternative Treatments
General consent requirement:
__ a disclosure of appropriate alternative procedures or courses of treatment that might be advantageous to the subject

Early feasibility consent recommendation:
describe the benefits, risks, and limitations of current treatment options

Other Information
General consent requirements: __ a statement describing the extent to which confidentiality of the subject's records will be maintained and that notes that FDA may inspect the records
__ for research involving more than minimal risk, an explanation as to whether any compensation and/or medical treatments are available if injury occurs and, if so, what they consist of or sources of further information
__ an explanation of whom to contact for answers to questions about the study and the subject's rights and whom to contact in the event of a research-related injury
__ a statement that participation is voluntary and that subjects may refuse to participate or discontinue participation at any time without penalty or loss of benefits, and whom to contact if they wish to withdraw

Early feasibility consent recommendation:

if applicable, include a statement that an investigator(s) has a proprietary interest in the test article and identification of the person the study subject can speak to about potential financial conflicts

Additional elements, when appropriate:

General consent requirements: __ a statement that the procedure or treatment may involve unforeseeable risks to subject, or to the embryo or fetus should the subject become pregnant

__ anticipated circumstances under which the investigator may terminate the subject's participation without regard to the subject's consent

__ any additional costs to subject as a result of participation

__ consequences of a subject's decision to withdraw and procedures for withdrawal

__ a statement that significant new findings developed during the course of research which may relate to the subject's willingness to participate will be provided to the subjects

__ the approximate number of subjects involved in the study

Early feasibility consent recommendations:

clearly indicate the consequences of withdrawal if, for example:

- withdrawal results in termination of therapies, testing, or monitoring; or
- transfer to an another health care provider is required if early termination of treatment and/or withdrawal from the study might adversely affect the subject, describe the specific procedures that are recommended to ensure the subject's safety and why these procedures are important to the subject's welfare

if continued follow-up is recommended to ensure the subject's safety following withdrawal, explicitly inform the subject of the potential adverse effects of premature termination and the need for continued follow-up

include a statement indicating that information will be provided to the study subject that may relate to the subject's willingness to participate

Appendix 4: Device iteration example

The following is a hypothetical scenario that illustrates the concepts described in Section 8 regarding device iteration during an early feasibility study.

Using the Pre-Sub process, a sponsor approaches FDA with a proposal to evaluate an innovative device in an early feasibility study to treat a disease common in the elderly. The device is unique in that delivery of the treatment will be through a catheter, rather than through the standard procedure which involves open surgery. The sponsor proposes to enroll up to 10 subjects at up to 3 investigational sites. The sponsor will evaluate the device performance and clinical outcomes after each subject is treated, and prior to enrolling the next subject.

In the Pre-Sub, the sponsor describes several potential device changes that may be implemented during the early feasibility study. The sponsor proposes the following specific iterative changes for which they will request contingent approval under the original early feasibility IDE, if the information obtained during the clinical study suggests that these device modifications are needed to optimize the device design:

- improvements in maneuverability, including:
  - modifying the shape of the nose cone of the introducer (e.g., increase or reduce tapering); and
  - making the sheath stiffer or more flexible;
- changing the length of the catheter to allow for the use of alternative access sites;
- modifying the hemostatic valve by changing material properties or device dimensions to improve hemostasis or reduce friction;
- implementing ergonomic changes in the handle that do not affect the overall function of the device (e.g., changing texture of knobs or handle); and • modifying the operator interface console.

During the Pre-Sub discussions, the sponsor and FDA reach agreement on the test plan to evaluate the proposed changes, including the acceptance criteria to be included in the original IDE application. Although some of these changes may be appropriate for 5-day notices, obtaining prospective, contingent approval under the original IDE will provide the sponsor with more predictability in the regulatory process for their device modification plans.

The sponsor, with help from the principal investigator, identifies other types of changes that may be needed for their device and clinical protocol during the conduct of their early feasibility study. In the original IDE application, the sponsor seeks FDA concurrence on their proposed approaches for implementing these changes, as outlined in Table 6.

Table 6: Regulatory process for anticipated modifications

Changes that may be appropriate for 5-day notification	**Changes that may be appropriate for contingent approval**	**Changes that may be appropriate for 30-day interactive IDE supplement**
Add a previously characterized surface coating to the catheter if lubricity is needed to improve access*	If a surface coating is added, modify the distribution, thickness or area covered by the coating	Expand the subject selection criteria (e.g., inclusion of younger subjects than defined in the original protocol)
Adding, moving, or changing the radiopaque bands on the catheter to improve visibility.	Improve the catheter resistance to kinking, with the type of modification and appropriate testing to be identified prior to supplement submission	Change from percutaneous access to open surgical access
Changes in the device preparation for use	Change the device to accommodate a broader range of subject anatomies (type of modification and therefore type of appropriate testing not identified in the original IDE)	
Add the use of an approved ancillary device (e.g., use of a longer introducer sheath) intended to improve the safety of the procedure*	Add new types of imaging studies to monitor device performance, if the modalities specified in the original protocol are found to be inadequate and if the new imaging procedure is supported through a risk assessment	
Modify the subject selection criteria to limit, rather than expand, the criteria*		
Modify procedural imaging modalities*		
Reduce follow-up assessments if early data support the change (i.e., the clinical data indicate that the change would not affect the safety of the subjects)*		
Change case report forms to capture additional information		

* These types of changes would not generally be appropriate for 5-day notification in a pivotal study due to their possible effect on the scientific soundness of the investigational plan and/or data validity.

FDA considers the proposed approaches to be reasonable.

The developmental device changes proposed for the 5-day notification process are considered appropriate in this case because they:

- are reasonably defined such that appropriate testing and expected outcomes are known;
- do not constitute significant changes in the basic principles of operation; and
- are not considered significant because they would not adversely affect the interpretability of the results of an early feasibility study, and would not be expected to adversely affect device

performance or to be associated with additional risk to the study subjects. Similarly, the clinical protocol changes would be appropriate for 5-day notification because the changes do not affect:

- subject safety, rights, or welfare;
- the validity of the data or information resulting from the completion of the approved protocol, because the data or information will not be pooled; or
- the relationship of likely patient risk to benefit relied upon to approve the protocol. The additional subject protection measures included in the early feasibility study protocol augment patient safety.

FDA recognizes that more types of changes are appropriate for 5-day notification during this early feasibility study than would normally be acceptable for a study enrolling a larger number of subjects or requiring a stable device design and clinical protocol to allow for pooling of the data from study subjects. For example, reducing the follow-up assessments would not likely be appropriate under a 5-day notice for a pivotal study; prior clinical studies would have been used to identify the appropriate follow-up assessments to ensure that consistent data are captured for each study subject. For this early feasibility study illustration, since the optimal study subject follow-up has not been defined, the sponsor plans to require laboratory testing on days 3, 7 and 14, but may find that, based on the results from the initial 5 subjects, the 7-day assessment is not informative and can be safely omitted. As the safety of subsequent study subjects would not be compromised with this change, FDA agrees that such a change during this study could be made with a 5-day notification.

During the course of the early feasibility study, the sponsor makes some of the anticipated changes, but also identifies an additional modification that had not been predicted in the original IDE submission. The sponsor proposes contingent approval for a change in a material used in the construction of their device based on obtaining acceptable results with the same types of nonclinical testing used to evaluate the original device design. To formally request this change, the sponsor submits an IDE supplement that describes the change and evaluation plan, including the acceptance criteria for the testing. FDA and the sponsor reach a consensus regarding the proposal during the 30-day review time for the supplement, and FDA grants approval of the modification, contingent on the successful completion of the test plan and reporting of the change and supporting information to FDA within 10 days of implementing the change. The sponsor evaluates the modified device according to the test plan, obtains acceptable results, implements the change and submits their test report to FDA 7 days after making the change.

Appendix 22: Reliance by another Institution on the Georgia Tech IRB

Occasionally, another institution, regardless of whether it has its own Office for Human Research Protections-approved Assurance, may wish to rely on the Georgia Tech IRB for review and oversight. The Georgia Tech IRB will accept such responsibility generally for a single project and only in cases meeting certain criteria:

- The Institutional Official approves the arrangement.
- The relationship between Georgia Tech and the other institution must result from a sponsored project agreement, subaward, or some other appropriate interaction.
- Georgia Tech and the relying institution will execute an Interinstitutional Agreement (IAAs) drawn by the Georgia Tech Office of Research Integrity Assurance. The IAA will stipulate the following:
    - The Georgia Tech IRB will follow written procedures for reporting its findings and actions to appropriate officials at the relying institution.
    - Relevant minutes of IRB meetings shall be made available to the relying institution upon request.
    - The relying institution will promptly and immediately forward to the Georgia Tech IRB any information regarding safety, adverse events, or other relevant data.
    - The relying institution will provide to Georgia Tech IRB any relevant correspondence between itself and the sponsor or the Office for Human Research Protections and the Food & Drug Administration.
    - The relying institution shall certify that it is not debarred from receiving federal funds and that its Assurance has not been suspended or terminated.
    - The relying institution remains responsible for ensuring compliance with the Georgia Tech IRB's determinations and policies and with the terms of its OHRP approved Assurance.
    - And any other criteria that are appropriate.
- When the relying institution is a recipient of federal funding, the relying institution must provide Georgia Tech with evidence that it holds a currently approved Assurance. Alternatively, the Georgia Tech Office of Research Integrity Assurance will verify existence and currency of the relying institution's Assurance by consulting the Office for Human Research Protections' website. The relying institution's record will be

printed by the Georgia Tech Office of Research Integrity Assurance and stored in the Interinstitutional Agreement file.
    - The relying institution shall provide documentation to the Georgia Tech Office of Research Integrity Assurance when its Assurance is renewed by OHRP during the life of the IAA.
- The relying institution's researchers must present documentation of having completed the required training in human research participant protections or, within thirty days of the execution of the IAA, satisfactorily complete the training provided by the Georgia Tech IRB.

Appendix 23: The Procedure: Translation of Documents

When consent forms, recruitment materials, or other documents must be translated into a foreign language, they should be reviewed and approved by the Institutional Review Board prior to being translated in order to avoid an additional translation expense. Translations for non-Exempt research must be accompanied by a certified affidavit of accurate translation from a professional translator service unaffiliated with the study. The Office of Research Integrity Assurance will obtain translations when necessary; the researcher/department will be responsible for the certification fee. Documents that have already been translated will be accepted for review if accompanied by a certified affidavit of accurate translation.

The same procedure applies when documents must be translated from another language into English, although IRB review cannot be conducted until the translation is accomplished.

Appendix 24: Sample Repository Submittal Agreement

A written agreement (Repository Submittal Agreement) is required for submission of data or materials to be submitted to Georgia Tech repositories, tissue banks, registries, data banks, or databases that have human subject involvement. The Repository Submittal Agreement to be utilized by the repository must undergo Institutional Review Board review and be approved prior to its use. The repository Principal Investigator or Guardian must ensure that an approved Repository Submittal Agreement is executed by the submitting investigator and maintained in the Georgia Tech Repository records.

GEORGIA INSTITUTE OF TECHNOLOGY
ENTER NAME OF REPOSITORY, TISSUE BANK, REGISTRY, DATA BANK, DATABASE
SUBMITTAL AGREEMENT

SUBMITTING INVESTIGATOR

Name: _____ Title: _____

Email: _____ Telephone: _____

Submitting Investigator's Institution Name: _____

Description of Data or Materials being submitted to the Repository for storage and use for future research.

Initial beside each of the conditions below that apply to this submission:

As Submitting Investigator, I certify that:

- ___ These data or materials were collected under a protocol approved by an Assured Institutional Review Board (IRB).
  - ___ The submitting institution's Federalwide Assurance number is provided here: _____
  - ___ A copy of the submitting institution's IRB approval letter is attached.
  - ___ A copy of the submitting institution's IRB-approved Consent Document for collection of these data or materials is attached.
- ___ There are no restrictions on the future uses of these data or materials.
- ___ There are restrictions on the future uses of these data or materials, as set forth below:

_____

_____

_____

— These data or materials were originally collected for clinical purposes.

— These data or materials are fully de-identified (not coded in any manner).

— These data or materials are coded. I will not provide the key to the code, nor will I provide access to the identities of subjects or to information through which their identities may be ascertained.

— These data or materials were collected under an IRB waiver of consent. I will not provide the key to the code, nor will I provide access to the identities of subjects or to information through which their identities may be ascertained.

— These data or materials were collected prior to April 13, 2003, thus subject authorization (under HIPAA) is therefore not required.

— These data or materials were collected under a HIPAA authorization or waiver requiring their destruction on or before this date: _____

— Data or materials from subjects declining to participate in future genetic research are
  - — excluded from the data or materials provided to this repository, or
  - — clearly marked for exclusion from future genetic research.

— Data or materials from subjects declining their use in future research, or who ask to be contacted prior to future use are
  - — excluded from the data or materials provided to this repository, or
  - — clearly marked for permission to be obtained prior to future use.

— I give my assurance that the data and materials being submitted are accurate to the best of my knowledge.

Submission accepted by Georgia Institute of Technology *name of repository, tissue bank, registry, data bank, database*.

_____ _____

Repository Principal Investigator or Guardian Signature

Name, printed

Date Accepted: _____

Appendix 25: Sample Repository Sharing Agreement

An IRB-approved written agreement (Repository Sharing Agreement) is required whenever data or materials will be distributed from Georgia Tech repositories, tissue banks, registries, data banks, or databases that have human subject involvement. The repository Principal Investigator or Guardian must ensure that the agreement is executed by the recipient investigator and maintained in the Georgia Tech Repository records.

GEORGIA INSTITUTE OF TECHNOLOGY
ENTER NAME OF REPOSITORY, TISSUE BANK, REGISTRY, DATA BANK, DATABASE
DATA/MATERIALS SHARING AGREEMENT

Recipient Investigator Name: _____ Title: _____

Email: _____ Telephone: _____

Recipient Investigator's Institution Name: _____

Describe here the data or materials being requested:

Check the applicable boxes regarding genetic information:
I am requesting data or materials that (*check one*):

- ☐ Involve genetics
- ☐ Do not involve genetics
- ☐ Involve both genetic and non-genetic components

As Recipient Investigator, I certify that the data or materials being shared with me will be used in accordance with the following conditions:

- The identities of subjects will not be disclosed to me, nor will I receive information through which their identities may be ascertained. If I request identifying information from the repository staff, it will not be provided. I will not attempt to contact individuals who are collecting the data or materials in order to obtain identifying information.
- If requesting data or materials that involve genetics, I will not use them for genetic research if they are marked for exclusion. I will verify that donors (subjects) have given specific consent for future genetic research; OR that data or materials from donors (subjects) who have opted out of future genetic research will be excluded from genetic studies or will be clearly marked so that the investigator can exclude them from the genetic portion of research.
- I will, within a reasonable period of time, notify the Repository Administrator or Principal Investigator of any relevant proposed changes in my research project and any unanticipated problems involving risks to subjects or others.
- I understand that use of these data or materials, if entirely within these conditions, does not require Georgia Tech's IRB approval. Any use beyond these conditions will require prior approval by the Georgia Tech IRB and possibly by an IRB at the recipient site.

Recipient Investigator Signature: _____ Date: _____

Appendix 26: Notice of the EU-UK GDPR

Effective May 25, 2018

What is the EU-UK GDPR and when does it take effect?

The European Union and United Kingdom General Data Protection Regulation ("EU-UK GDPR") is a new and more stringent regulation governing the use of personal data. It imposes new obligations on entities that control or process personal data about people who are located in the European Union and the United Kingdom. This regulation applies both inside the European Union ("EU"), United Kingdom ("UK"), *and* outside of the EU and UK, and applies to data about anyone in the EU and UK, regardless of whether they are a citizen or permanent resident of an EU or UK country.

The regulation took effect on May 25, 2018.

What information is subject to the EU-UK GDPR?

The EU-UK GDPR applies to the control or processing of 'personal data,' which is defined as:

> Any information relating to an identified or identifiable natural person (the data subject); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, psychological, genetic, mental, economic, cultural or social identity of that natural person.

Examples of identifiers include but are not limited to: name, photo, email address, identification number such as GT ID#, GT Account (User ID), physical address or other location data; IP address or other online identifier.

What does this mean to YOU as a GT researcher?

If you obtain personal data about any human subject or research collaborator located in the European Union, this policy applies to your research.

Please refer to the following links for further details:

- **Institute GDPR Compliance Policy**
- **GT's Institutional Review Board EU-UK GDPR Privacy Notice**
- **GT's Institutional Review Board EU-UK GDPR Consent Form for Sensitive Personal Data**

GLOSSARY

Reviewed: July 2024

Adverse events:

1. An Adverse Event is an unfavorable event associated with the study interventions. Such events may be anticipated or unanticipated. An adverse event includes adverse drug experiences, adverse device effects, and problems involving harm to human subjects. (For example, adverse events include allergic reaction, hospitalization, supply problems with protocol-specific materials, or theft of a laptop computer that contains study identifiers, etc.).
2. A Serious Adverse Event is one that is fatal, life-threatening, persistent, significantly disabling or incapacitating, requires inpatient hospitalization or prolongation of hospitalization, results in congenital anomaly or defect, and/or that is a significant medical incident. (A significant medical incident is considered a serious, study-related adverse event because, it may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.)
3. An Unanticipated Adverse Event is one that results from a study intervention and was not expected or anticipated from prior experience. An Unanticipated Adverse Event can include expected adverse events that occur with greater frequency or severity than predicted from prior experience. It is possible for an adverse event to be characterized as serious and unanticipated.

Anonymous Samples: Specimens lacking any code or identifier that would allow a link back to the subject who provided it.

Applicable Clinical Trial (ACT): Under Section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA 801), the United States Congress defined an "Applicable Clinical Trial" as an applicable device clinical trial or an applicable drug clinical trial (both listed below). These terms became codified at section 402(j) of the Public Health Service (PHS) Act, and include conforming amendments to the Federal Food, Drug, and Cosmetic FD&C Act (FD&C Act).

Applicable Device Clinical Trial: The term 'applicable device clinical trial' means:

i a prospective clinical study of health outcomes comparing an intervention with a device subject to section 510(k), 515, or 520(m) of the Federal Food, Drug, and Cosmetic Act against a control in human subjects (other than a small clinical trial to determine the feasibility of a device, or a clinical trial to test prototype devices where the primary outcome measure relates to feasibility and not to health outcomes); and

ii a pediatric postmarket surveillance as required under section 522 of the Federal Food, Drug, and Cosmetic Act.

a. Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, 121 Stat. 904 (2007).

Applicable Drug Clinical Trial: The term 'applicable drug clinical trial' means a controlled clinical investigation, other than a phase I clinical investigation, of a drug subject to section 505 of the Federal Food, Drug, and Cosmetic Act or to section 351 of this Act.

i "Clinical Investigation": For purposes of subclause (I), the term 'clinical investigation' has the meaning given that term in section 312.3 of title 21, Code of Federal Regulations (or any successor regulation).

ii "Phase I": For purposes of subclause (I), the term 'phase I' has the meaning given that term in section 312.21 of title 21, Code of Federal Regulations (or any successor regulation).

a. Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, 121 Stat. 904 (2007).

Authorization: Authorization is the HIPAA equivalent of consent to use and disclose data.

Case Report Form: A record of data collected about each participant in a clinical trial; data are used by sponsor or sponsor-investigator to test hypothesis or to answer research question.

Clinical Study: Under §42 CFR 11, a "Clinical Study" is defined as "research according to a protocol involving one or more human subjects to evaluate biomedical or health-related outcomes, including interventional studies and observational studies.." This term is interchangeable with "Clinical Investigation" and "Clinical Research."

Clinical Trial: Under §42 CFR 11, a "Clinical Trial" is defined as "a clinical investigation or a clinical study in which human subject(s) are prospectively assigned, according to a protocol, to one or more interventions (or no intervention) to evaluate the effect(s) of the intervention(s) on biomedical or health-related outcomes."

Combination Product: A product composed of any combination of a drug and a device; a biological product and a device; a drug and a biological product; or a drug, device, and a biological product.

Co-Principal Investigator: Individuals who share the responsibility for the study with the Principal Investigator and therefore requires the same qualifications as for PI.

Co-Investigator: This title designates key personnel for a project, but without the oversight responsibility of a Principal Investigator.

Consideration: Value exchanged to create a contract.

Covered Entity: Covered entities are health care providers, health plans, and health care clearinghouses.

Data and Safety Monitoring Board (DSMB): Also called a "Data Monitoring Committee" (DMC), a DSMB is an independent committee that conducts ongoing review of data to assure subject safety.

Data Safety Monitoring Plan: A plan written to ensure that the relevant data are collected and assessed to monitor subject safety within a study. Part of the DSMP may be the establishment of a Data and Safety Monitoring Board, but is not necessarily required for every DSMP.

Data Use Agreement: The official agreement between the provider and recipient of Protected Health Information (PHI) collected under a protocol. The agreement defines the PHI, states whether it qualifies as a Limited Data Set, and names the persons (or positions) authorized to have access to the Protected Health Information collected in the study. Other terms and conditions may apply.

Experimental Subject: The Department of Defense definition is: An activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction [32CFR.210.102 (f) reference (c)]. Examples of interventions or interactions include, but are not limited to, a physical procedure, a drug, a manipulation of the subject or subject's environment, the withholding of an intervention that would have been undertaken if not for the research purpose.

FERPA: The Family Educational Rights and Privacy Act (FERPA) (20 U.S.C. § 1232g; §34CFRPart 99) is a Federal law that protects the privacy of student education records. The law applies to all schools that receive funds under an applicable program of the U.S. Department of Education.

Finder's Fee: A small fee paid to individuals who refer willing human subject research participants.

Genetic Research: any research involving the analysis of human DNA and chromosomes as well as biochemical analysis of proteins and metabolites when the intent of the research is to collect and evaluate information about heritable disease and/or characteristics within a family.

Guardian: An individual authorized under applicable State or local law to consent on behalf of a child to general medical care when general medical care includes participation in research. Can also be an individual who is authorized to consent on behalf of a child to participate in research. **NOTE:** In 2013, the Food and Drug Administration revised its definition of *Guardian* at 21 CFR 50.3(s) as follows: *"Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care."*

HIPAA: Health Insurance Portability and Accountability Act (HIPAA): The Department of Health and Human Services' *National Standards to Protect the Privacy of Personal Health Information* are promulgated in the Health Insurance Portability and Accountability Act (HIPAA), commonly referred to as the "Privacy Act." This Act specifies requirements for protection of individually identifiable health information, or "protected health information" (PHI). See Appendix 10 for a complete discussion of HIPAA and the procedures to comply at Georgia Tech.

Human Subject: A *human subject* is a living individual about whom an investigator conducting research obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. Included in the definition of human subject are human embryos, fetuses, and any human tissue or fluids. Thus, the scope of *human subject* is interpreted broadly. If you are interviewing people, looking at medical records or conducting a survey, you are involving human subjects in your research. *See Appendix 15 for an important distinction in this definition for research involving DOD.*

Hybrid Entity: An organization where some parts are subject to HIPAA, while others are not. In such cases, the Privacy Rule applies only to specified units.

Identifiable/Coded Samples: specimens that can be linked back to the subject who provided them.

Identifier: Information that links specimens or data to individually identifiable living people or their medical information. Examples include names, social security numbers, medical record numbers, and pathology accession numbers.

Legally Authorized Representative: An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

Lotteries and Raffles: The Georgia Code defines lotteries and raffles as "any scheme or procedure whereby one or more prizes are distributed by chance among persons who have paid or promised consideration for a chance to win such prize." This definition encompasses almost any contest in which something is given away, as long as the participant is required to provide something of value ("consideration"), in exchange for the chance to win.

Minimal risk: Defined in §45CFR46.102 as "the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests." FDA defines *minimal risk* as the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

NIH Clinical Trial: NIH defines a clinical trial as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. (See NOT-OD-15-015: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-015.html).

- Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies.

Prisoner: Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

Principal Investigator: The individual responsible for the conduct of the study.

Prospective Collection: specimens do not exist 'on the shelf' when request is made to Georgia Institute of Technology IRB for approval.

Protected Health Information (PHI): Protected health information includes all *individually identifiable* health information transmitted or maintained by an organization covered by the HIPAA regulations (a "covered entity"), regardless of form. Specifically, if it is Individually Identifiable Health Information (IIHI) that is:

- created or received by a health care provider, health plan, employer, or health care clearinghouse; and
- personal health information that relates to:
  - the past, present, or future physical or mental condition,
  - the past, present, or future provision of care to an individual, or
  - the past, present or future payment for provision of health care to an individual, and identifies the individual (or there is a reasonable basis to believe that the information can be used to identify the individual).

Research: A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. The definition also includes research development, testing and evaluation, and research undertaken by students for the purpose of independent study, theses or dissertations.

Research (DoD): Department of Defense Instruction (DoDI) 3216.02 definition of "research" and "experimental subject" -- "An activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction (32 CFR 219.102(f), reference (c))."

Research Setting: The research site and the IRB responsible for that site.

Retrospective Collection: proposed research involves using specimens that already exist, i.e., already collected and are 'on the shelf', stored or frozen at time of protocol submission to Georgia Institute of Technology IRB.

Sponsor: A person who initiates a clinical investigation, but who does not actually conduct the investigation, i.e., the test article is administered or dispensed to or used involving a subject under the immediate direction of another individual. A person other than an individual (e.g., corporation or

agency) that uses one or more of its own employees to conduct a clinical investigation it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.

Sponsor-investigator: An individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., corporation or agency.

Support: *Department of Defense Instruction (DoDI) 3216.02,* defines "support" as generally meaning "the provision of funding, personnel, facilities, and all other resources."

Test article: Any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n).

Third Party: Refers to tissue that is not obtained from the human subject directly, but via another source, i.e., tissue bank, Department of Pathology etc. The third party may have the tissue coded with respect to subject identity, but the investigator receives the tissue in an anonymous manner, i.e., no way to link the subject's identity to the tissue once it is in the investigator's hands.