The Masgutova Graduate School of Neurodevelopmental Sciences

Investigator Manual

Effective January 2025

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The Masgutova Graduate School of Neurodevelopmental Sciences

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Scope

Throughout this document, "Institution" refers to The Masgutova Graduate School of Neurodevelopmental Science. Defined terms can be found in HRP-001 - SOP - Definitions.

1. What is the purpose of this manual?

This document, HRP-103 - INVESTIGATOR MANUAL, is designed to guide you through the policies and procedures related to the conduct of human subjects specific to this Institution. For clarity, within this manual, most uses of the capitalized word "Institution" refer to MGS. The lower-case word can mean any other institution.

General information regarding human subjects research protections and relevant federal regulations and guidance is incorporated into the required human protection training. For additional information see Question #4 of this Investigator Manual.

2. What is human subject's research?

The HRP-101 - HUMAN RESEARCH PROTECTION PROGRAM PLAN defines the activities that this Institution considers to be human subjects research. A tool for determining whether an activity is human subjects research can be found in the HRP-310 - WORKSHEET - Human Subjects Research Determination as well as a Human Research Determination Survey, located in the electronic IRB system (MGS IRB) Library. Use this document and for guidance as to whether an activity meets either the DHHS or FDA definition of human subjects research, keeping in mind that the IRB makes the ultimate determination in questionable cases as to whether an activity constitutes human subjects research subject to IRB oversight.

You must not conduct human subjects research without prior IRB review and approval. This includes exempt human subjects research determinations that must be made by the IRB Office. If you have questions about whether an activity is human subjects research, contact the IRB Office at IRB@mgsns.org

3. What is the Human Research Protection Program?

The document HRP-101 - HUMAN RESEARCH PROTECTION PROGRAM PLAN, found in MGS IRB library, describes this institution's overall plan to protect subjects in human subjects research and includes:

- The mission of the Human Research Protection Program (HRPP).
- The ethical principles that the institution follows governing the conduct of human subjects research.
- The applicable laws that govern human subjects research.
- When the institution becomes engaged in human subjects research and when someone is acting as an agent of the institution conducting human subjects research.
- The types of human subjects research that may not be conducted.
- The roles and responsibilities of individuals within the institution.
- MGS Human Research Protection Program:
    - The Institutional Review Board (IRB)

    - IRB Program staff
        - Biomedical IRB Manager
        - Social Behavioral IRB Manager
        - Reliance Manager
        - Research Compliance Administrators (RCAs)
    - The IRB Education Program
    - The Quality Assurance/Quality Improvement (QA/QI) Program
    - The IND/IDE Assistance Program (revisions pending)
    - The HIPAA Research Compliance Program
- Human Research Protection Program Supporting Programs:
    - The Conflict of Interest (COI) Program and Committee
    - The Institutional Biosafety Program/Committee (IBC)
    - The Radiation Safety Program/Committee
    - The Export Controls Office
    - Sponsored Research (SR)
    - Technology Transfer Office/Patents and Licensing (TTO)
    - The Office of Clinical Research (OCR) – MGS Health
    - Office of Community Engagement and Partnerships (OCEP)
- HRPP Institutional Administration:
    - President of MGS
    - Provost of MGS

4. What training do my staff and I need to conduct human subjects research?

This section describes the training requirements imposed by the IRB. You may have additional training imposed by other federal, state, or institutional policies. It is your responsibility to know which training requirements apply to your research.

Investigators and staff conducting research involving human subjects research must complete human subjects protection (HSP) education. This requirement extends to anyone engaged in the research, including individuals who collect data about human subjects, those conducting study procedures or interventions, and those who have access to private, identifiable information. This requirement applies to all human subjects research regardless of funding or source of sponsorship. Members of the research team who have not completed HSP training may not be engaged in human subjects research. The MGS IRB has the authority to suspend or withhold approval of projects that involve investigators and research personnel who fail to meet the education requirements as outlined in this policy.

Training is valid for a three (3) year period, after which time the training must be repeated or a refresher course taken.

Study staff must complete one (2) of the following courses:

From the Human Research Protection Foundational Training | HHS.gov

- When HHS Regulations Apply (Lesson 1)

- What is Human Subjects Research (Lesson 2)
- What are IRBs (Lesson 3)
- IRB Review of Research (Lesson 4)
- Institutional Oversight of Human Research (Lesson 5)

From the Human Research Protection Training | HHS.gov

- Participant-Centered Informed Consent Training
- Considerations for Reviewing Human Subjects Research

Certificates of completion are provided after each training session. Certificates must be presented at the time of IRB submission.

5. What financial interests do my staff and I need to disclose to the MGS IRB?

Financial conflicts of interests are related to a research project if the work to be performed on the project, or the results of such work, can be expected to have an effect on the individual's interest(s), financial or a perception of later potential financial gains. Institutional conflicts of interest are situations in which the financial interests of this Institution or any individual acting in his or her authority on behalf of the Institution, may affect or appear to affect the research conducted under the auspices of the Institution. All study team members/research personnel are required to disclose individual or institutional conflicts of which they are aware of and related financial interests for themselves, their spouse, domestic partner, and dependent children in MGS IRB:

- On submission of an initial review;
- At least annually as part of continuing review if applicable; and/or
- Within thirty (30) days of discovering or acquiring (e.g. through purchase, marriage, or inheritance) a new financial interest.

Additional details, including thresholds for disclosure, can be found in HRP-055 – SOP - Financial Conflicts of Interest and HRP-054 – SOP - Institutional Conflicts of Interest.

All individuals involved in the design, conduct, or reporting of research are required to disclose their financial interests during the IRB submission process.

6. How do I submit new human subjects research to the IRB?

Once you have determined that your project meets the definition of research, review the applicable regulations and policies, and create your study documents using the appropriate templates. Protocol and informed consent templates are located in the MGS IRB Library. Guidance documents and links to step-by-step videos can be found in the Regulations and Guidance section of the MGS IRB homepage.

Information related to writing a protocol and creating an informed consent document can be found in Question #11 and Question #20 of this Investigator Manual.

All individuals who will be engaged in the research must have an MGS student account in order to be listed. Included within your account, you will need to have a current CV/resume that shows an MGS affiliation and current training as described in Question #4.

Please note, individuals with MGS courtesy faculty appointments may be Investigators, but may not serve as a Principal Investigator on IRB research applications.

Maintain electronic copies of all information submitted to the IRB in case revisions are required. Before submitting the research for initial review, you must:

- For student researchers, include your faculty advisor as a member of the study team in the consent document.
- Document the financial interest status ("yes" or "no") of each research member.
- Document the agreement of research staff to his/her role in the research.

7. Who needs to review my research before I submit it to the IRB?

The IRB requires scientific and scholarly review to be conducted by the department or affiliate for all human subjects research prior to being presented to the IRB or other relied upon IRBs with which the institution has contracted to provide IRB oversight. It is the responsibility of the Investigator to select their department and/or the applicable affiliate institution to ensure that scientific and scholarly review is obtained for each new research proposal involving human subjects prior to submission to the IRB or relied upon IRBs.

Criteria for scientific and scholarly review of the IRB application and study protocol for human subjects' research are outlined in HRP 320 – WORKSHEET - Scientific or Scholarly Review. The Department/Affiliate Reviewer may send requested revisions to the Investigator in MGS IRB. Once the Scholarly review is complete and the protocol found to be acceptable, the completed worksheet HRP-320 should be uploaded into MGS IRB as an attachment within the Ancillary Review. The Department/Affiliate Reviewer should be an individual who is not directly associated with the proposed research.

8. How do I request to use an external IRB?

If an external IRB is to be used, please make sure to contact the MGS IRB at IRB@mgsns.org , early in the process to ensure there is ample time to process the required agreements prior to the start of the research.

The IRB Chairperson or designee will determine, on a study-by-study basis, whether reliance on an external IRB is appropriate. In deciding whether or not to rely on an external IRB, chairperson or designee will consider such factors as:

- Whether the use of a single IRB (sIRB) has been mandated by the study sponsor;
- The number of proposed studies involved in the collaboration;
- The anticipated level of risk associated with the proposed study;

- Whether the Reviewing IRB's policies and procedures meet the MGS IRB's standards. If the Reviewing IRB is part of an AAHRPP-accredited HRPP, then it will be presumed that the IRB's standards are being met. However, AAHRPP accreditation in and of itself does not necessarily suffice as a basis for reliance;
- The location in which the majority of study procedures will take place;
- The Investigator's standing with the Graduate School and role in the overall research;
- The ability of the Reviewing IRB to be sufficiently informed about local context issues, including local laws and regulations; and
- The terms and conditions of the proposed IRB reliance agreement.

Once the MGS IRB has agreed to reliance on an external IRB, submit the IRB proposal form to MGS IRB, indicating that an external (Reviewing) IRB will serve as the IRB of Record and attach all requested documents. The Investigator is the only individual that can submit. Maintain electronic copies of all information submitted to the IRB in case revisions are required.

Investigators seeking to rely on an external IRB are responsible for providing the following documentation within MGS IRB:

- For industry-sponsored research being reviewed by commercial IRBs:
    - The study protocol and informed consent document(s) that include this Institution's template subject injury, privacy and confidentiality, DNA and HIPAA authorization language, as appropriate;
- For research being reviewed by academic or other IRBs:
    - The approved study protocol and informed consent templates. The templates must be revised to include this Institution's template subject injury, privacy and confidentiality, DNA and HIPAA authorization language, modified as applicable for the research;
    - Contact information for the Reviewing IRB in order for the MGS IRB to initiate conversations regarding the IRB reliance agreement;
    - Documentation of the initial or most recent continuing review approval by the external IRB .

The MGS IRB does not execute a formal IRB reliance agreement for research determined to be exempt, except when the exempt research requires a limited IRB review. For research that has been determined to be exempt by an external IRB, the protocol will have to be reviewed and approved by the local IRB to obtain the exempt determination.

The MGS IRB does not execute IRB reliance agreements for non- research (i.e. compassionate use, expanded use). The research team needs to reference Question #39 for the submission process.

9. How do I request the MGS IRB to serve as the single IRB (sIRB) of record for my collaborative or multi-site research study?

If you will request that MGS IRB serve as the reviewing IRB (sIRB) for cooperative research, contact the MGS IRB Chairperson prior to submitting grant or other funding applications to determine whether this IRB will agree to serve as the sIRB for the study. At this time, the MGS IRB is only serving as a sIRB for federally funded projects where MGS is the prime awardee and the funding agency requires the use of a sIRB. The MGS Investigator is required to contact the MGS IRB Reliance Manager to generate an IRB budget that is to be included within the funding proposal. When it is determined that another institution will rely on the MGS IRB, is engaged in human subjects research, and possesses a Federalwide Assurance (FWA), an IRB reliance agreement between that institution and MGS must be established prior to the initiation of research activities at the site. The IRB Reliance Manager will work with the MGS PI to begin the process of documenting reliance with the additional institutions. The relying institution and the MGS IRB will each maintain the fully executed IRB reliance agreement for inspection by OHRP, as requested. An FWA is required for all sites receiving Public Health Service (PHS) funding for the conduct of research.

If the proposed research is exempt, even if federally funded, the MGS IRB will not be able to serve as a sIRB for any additional sites. All other sites will need to submit to their local IRB for approval of their activities.

Please contact the MGS IRB at IRB@mgsns.org , early in the process to ensure there is ample time to process the required agreements prior to the start of the research.

Once approved by the Chairperson or Designee, submit the single IRB project within MGS IRB, indicate that the study is a multi-site or collaborative research study, by selecting “yes” to the question “Will the MGS IRB act as the single IRB of record for other participating sites?”

See also Question #12 of this Investigator Manual for collaborative research with MGS as the Coordinating or Data Center. It is not considered a single IRB activity.

10. How do I transfer IRB Oversight?

Prior to entering into any agreement to transfer a study to another IRB, the study Investigator must contact the MGS IRB Chairperson at IRB@mgsns.org , to discuss the proposed transfer.

Please review Question #8 of this Investigator Manual that details the process to use an external IRB. Be aware this will require a new external application submission to document the change in MGS oversight related to the project. Once the external application is approved the research team will need to close out the original MGS application.

The MGS IRB may also agree to assume responsibility for oversight of research previously approved by an external IRB. The MGS IRB may require that a plan for the transfer process be documented in a written agreement between the original and receiving IRBs. Such agreement will address how the IRBs will manage and document the following: 1) identifying the study(ies) for which IRB oversight is being transferred; 2) ensuring the availability and retention of

pertinent records; 3) establishing an effective date for transfer of oversight, including records, for the study(ies); 4) conducting a review of the study(ies) by the receiving IRB, where appropriate, before it accepts responsibility for the study(ies); 5) confirming or establishing the date for the next continuing review; 6) determining whether the consent form needs to be revised; and 7) notifying the key parties.

11. How do I write an Investigator Protocol?

Use the HRP-503 - Biomedical Protocol Template, HRP-503a- Social-Behavioral Protocol Template or HRP-504- Record Review Protocol Template as a starting point for drafting a new Investigator Protocol, and reference the instructions in italic text for the information the IRB looks for when reviewing research. MGS investigators are required to use a MGS protocol template for their research. Here are some key points to remember when developing an Investigator Protocol:

- The italicized bullet points in the HRP-503, 503a and 504- Protocol Templates serve as guidance to investigators when developing an Investigator Protocol for submission to the IRB. All italicized comments/directions should be deleted prior to submission.
- For industry-sponsored studies or multi-site studies for which the MGS Investigator is not the lead Investigator, use the local protocol supplement document HRP-508 or HRP-508a - Site Supplement Protocol Template. For any items described in the main Investigator's or sponsor's protocol or other documents submitted with the application, investigators may simply reference the page numbers of these documents within the Investigator Protocol rather than repeating information.
- When writing an Investigator Protocol, always keep an electronic copy. You will need to modify this copy when making changes to the Investigator Protocol.
- If you believe your activity may not be human subjects research, please review the "Comparison Chart- Human Subjects Research Quality Improvement Program Evaluation Class Projects" guidance document located in the Regulation and Guidance section of the MGS IRB homepage. If you have additional questions, please contact the IRB Office, at IRB@mgsns.org prior to developing your Investigator Protocol and submitting an application in MGS IRB.
- Note that, depending on the nature of your research, certain sections of the template may not be applicable to your Investigator Protocol. Indicate this as appropriate with "N/A" after the section number.
- You may not involve any individuals and/or their data who are members of the following populations as subjects in your research unless you indicate this in your inclusion criteria; the inclusion of subjects in these populations has regulatory implications.
    - Adults unable to provide legally effective consent (i.e. cognitively impaired)
    - Individuals who are not yet adults (infants, children, teenagers <18 years)
    - Pregnant women
    - Prisoners
- Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic

minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.

- If you are conducting community-based participatory research, you may contact the IRB Office for information about:
  - Research studies using a community-based participatory research design
  - Use of community advisory boards
  - Use of subject advocates
  - Partnerships with community-based institutions or organizations
- If the research will utilize a third party for the transcription of audio or video recording, the Investigator must include information within the consent document detailing the types of data/recordings the third party may have access to, such as any identifiable data that is discussed or shown within the recordings.
- Refer to Question 37 of the Investigator Manual and the "Retention and Destruction of Research Records" guidance document for located in the Regulation and Guidance section of the MGS IRB homepage to ensure you are following MGS IRB research data storage requirements.

Sharing Research Laboratory Results with Subjects

This Institution complies with Clinical Laboratory Improvement Act (CLIA) requirements. Under the current interpretation of these requirements, the Institution will not permit nor approve a plan for researchers to disclose or report results of research tests when such tests have been performed in laboratories that have not been CLIA-certified. This Institution's IRB may approve a request on a case-by-case basis to allow all subjects to receive a form letter indicating that clinical testing is now available and they may wish to have testing conducted at a certified clinical laboratory.

12. How do I submit an application for a Coordinating or Data Coordinating Center?

If MGS is serving as both a Coordinating Center and clinical site enrolling subjects, two separate applications must be submitted within MGS IRB – one for the Coordinating Center and another for the clinical site.

13. Do case reports or limited case series need to be submitted to the IRB?

A case report or limited case series is a description of the characteristics, evaluation, and/or treatment(s) of a single individual or a small group of individuals that share a common condition, but did not involve activities defined as research. The subject(s) of the case(s) may be patients, clients, students, or other individuals who have been evaluated, treated, counseled, or taught.

The retrospective review of records for publication of a single case report or a limited case series involving data from three (3) or fewer individuals is not considered to be research involving human subjects, and therefore such a report does not require IRB review and approval. The IRB

regards case reports or a limited case series as an educational activity, and therefore it is permissible under the Health Insurance Portability and Accountability Act (HIPAA) as a part of health care operations (45 CFR 164.501) when reviewing medical records.

The use of a single subject in prospective research activity (n = 1) does constitute research that is subject to IRB review and approval when there is a clear intent before recruiting or interacting with the subject to use systematically collected data or information.

14. Do I need a data and safety monitoring plan (DSMP)?

Studies that pose greater than minimal risk to subjects must include a DSMP. A Data Safety Monitoring Board (DSMB) may also be required if the study involves blinding, multiple sites, vulnerable subjects, or employs high-risk interventions. The NIH requires the establishment of DSMBs for all Phase III multi-site clinical trials involving interventions that entail potential risk to the subjects.

15. What if I am doing my research at a non-MGS (or non-affiliate) location?

MGS investigators at times may conduct research at sites that are not owned or operated by this Institution or its affiliates. During the course of reviewing the protocol, Investigators must provide the IRB with information regarding the facility and population to be recruited. A letter of support from the site where the research will be conducted is required by the IRB. A letter of support is also required of an organization providing the Investigator with private information (e.g. contact information) about their employees, students, etc. for recruitment purposes.

Investigators are responsible for ensuring the administrator signing the letter of support understands the IRB's expectations of him/her and has the authority to make those assurances. Letters of support must be printed on the facility's letterhead and signed by the administrator. Alternatively, an email that contains the organization's logo and the administrator's signature is acceptable. The letter or email must include the following:

- A statement that the site administrator has reviewed the research and has found it appropriate for the population of that facility;
- A statement allowing the Investigator to conduct the research activities on site and if applicable, indicating there are appropriate resources available to conduct the research;
- Contact information for an individual who will represent the facility in matters related to the conduct of human subjects research; and
- A statement that based on the risks associated with the research, there are adequate provisions to handle unanticipated problems and/or adverse events as applicable.

If the external institution has an IRB, or similar review committee, the external institution should provide documentation that the research has been reviewed and approved by that committee. In situations where MGS is relying upon the external IRB for the review and approval of the research project, or conversely, if the external institution is relying on the MGS IRB for the

review and approval of the research, the local study team must complete a new IRB submission through MGS IRB, noting that either the MGS IRB or an external IRB will act as the IRB of record for the study.

16. What if I am doing my research outside of the country?

The Office of Human Research Protections (OHRP) provides guidelines that govern human subjects research in foreign countries, as well as standards from a number of international and regional organizations. The MGS HRPP requires researchers to comply with these guidelines when conducting international research. For more information regarding these guidelines, please see http://www.hhs.gov/ohrp/international/intlcompilation/intlcompilation.html.

International research that involves the enrollment of children should consider the following:

- If the child is considered an adult in the country in which the research is taking place;
- The relationship between parents and their children and whether or not there is an acceptable and effective parental permission process;
- If the assent of the child is permissible by local customs; and
- If there are laws pertaining to the enrollment of parentless children in research.

In addition to ensuring equivalent protections encompassing the ethical principles of respect for persons, beneficence, and justice, investigators conducting human subjects research outside the U.S. are responsible for the following:

- Obtain local IRB approval see Question #8 to describe the process for using an external Ethics Committee. Demonstrate approval from the local Ethics Committee (or similar committee) should one exist in the host country in which the research will be conducted. If an Ethics Committee does not exist, then a letter of support from a community leader or the local government must be obtained.
- Have the knowledge of and comply with local laws, regulations, political or socio-economic factors, and cultural context while conducting research. Care must be taken to ensure that the cultural norms of the host country are respected and that the subjects will not suffer adverse consequences from participation, such as being subjected to retaliation from local authorities or the local community. If the researcher is unfamiliar with the local laws, cultural norms, etc., he/she must involve a local collaborator in the conduct of the research.
- Implement an informed consent process that is consistent with the cultural norms of the country in which the research will be conducted. The informed consent document should be translated into a language that is understandable by the subject. Please see Question #20 of this Investigator Manual for more information on informed consent requirements when conducting research with non-English speaking participants.

- If the Investigator does not speak the language of the country in which the research will be conducted, he/she must describe how communication with subjects will be conducted.
- Assist colleagues from the host country in obtaining a FWA if the research is federally funded and requires that the transnational institution receive an approved FWA from OHRP.
- Determine if an export license is required by contacting the MGS IRB office (IRB@mgsns.org) Scenarios in which this may be required include:
    - A physical transfer/disclosure of an item outside the U.S.;
    - Any transfer/disclosure of a controlled item or information within the U.S. to a foreign national;
    - Participation of foreign national faculty, staff, or student in the research;
    - Presentation/discussion of previously unpublished research at conferences or meetings where foreign national scholars may be in attendance;
    - Research collaborations with foreign nationals and technical exchange programs;
    - Transfers of research equipment abroad; or
    - Visits to the local Investigator's lab by foreign national scholars.
- Determine if the research involves a Foreign Country of Concern (FCOC) and the MGS IRB will refer to the Office of Foreign Assets Control (OFAC). Contact IRB@mgsns.org to begin the process of obtaining all appropriate approvals **prior** to submitting an application to the IRB.
- Review the U.S. Department of State's U.S. Passports & International Travel website for a current list of noted high-risk countries and travel warnings and alerts. If any member of the study team is traveling to a noted high-risk country, the Investigator should contact the Export Controls Office prior to traveling to the host country.

17. Are there any Florida Laws that I should be aware of that might affect my research plan?

The Investigator is responsible for complying with Florida state laws and regulations as applicable in the conduct of human subjects research. The IRB, IRB Chairperson, or designees are responsible for ensuring proposed human subjects research is in compliance with Florida state laws and regulations, when applicable, prior to issuing approval.

The following Florida Statutes will be applied to human subjects research, when applicable:

HIV Testing (Florida Statutes §381.004)

This law establishes the parameters for consent and disclosure of results relating to HIV testing in Florida and applies to all human research where an HIV test will be performed during either the eligibility screening or the research study itself. Informed consent for HIV testing is mandatory and must include:

- A prior explanation of the right to confidential treatment of the information identifying the subject and the results of the test to the extent provided by law;
- A disclosure that a positive HIV test result will be reported to the county health department with sufficient information to identify the subject;
- The availability and location of sites where anonymous testing is performed (each county health department maintains a list of sites at which anonymous testing is performed).

Reasonable efforts must be made to notify the subject of the results. If the test is positive, notification must include information on the availability of appropriate medical and support services, the importance of notifying partners who may have been exposed, and the prevention of transmission of HIV. A positive preliminary test result may not be revealed to any person except:

- The licensed physicians or the medical or nonmedical personnel subject to the significant exposure;
- Health care providers and to the person tested when decisions about medical care or treatment of, or recommendation to, the person tested and, in the case of an intrapartum or postpartum woman, when care, treatment, or recommendations regarding her newborn, cannot await the results of confirmatory testing. Positive preliminary HIV test results may not be characterized to the patient as a diagnosis of HIV infection. Please see also Question #11 of this Investigator Manual regarding CLIA requirements when sharing lab results with subjects.

The results of rapid testing technologies shall be considered preliminary and may be released in accordance with the manufacturer's instructions as approved by the federal Food and Drug Administration. Corroborating or confirmatory testing must be conducted as follow up to a positive preliminary test. Results shall be communicated to the subject according to statute regardless of the outcome. If the test is negative, notification must include, as appropriate, information on preventing the transmission of HIV.

The identity of the subject and the test results are confidential and may not be disclosed except to:

- The subject or the subject's legally authorized representative;
- Someone with a legally effective release for HIV test results executed by the subject or the subject's legally authorized representative (a general release or subpoena does not permit the release of HIV testing or HIV test results);
- An authorized agent or employee of a health facility or health care provider if the health facility or health care provider itself is authorized to obtain the test results, the agent or employee participates in the administration or provision of patient care or handles or processes specimens of body fluids or tissues, and the agent or employee has a need to know, as defined by the Department of Health;
- Health care providers consulting between themselves or with health care facilities to determine diagnosis and treatment;
- The Department of Health/county health department;

- Authorized medical or epidemiological researchers who may not further disclose any identifying characteristics or information;
- Others as specified by statute.

Disclosure of test results to anyone on the exception list must be accompanied by the following statement: "This information has been disclosed to you from records whose confidentiality is protected by state law. State law prohibits you from making any further disclosure of such information without the specific written consent of the person to whom such information pertains, or as otherwise permitted by state law. A general authorization for the release of medical or other information is NOT sufficient for this purpose."

Capacity of Principal; Procedure (Florida Statutes §765.204)

This law states the criteria for determining whether an individual is capable of giving informed consent. An individual is presumed to be capable of making health care decisions for herself or himself unless she or he is determined to be incapacitated. Incapacity may not be inferred from the person's voluntary or involuntary hospitalization for mental illness or from her or his intellectual disability. If an individual's capacity to make health care decisions for herself or himself or provide informed consent is in question, the primary or attending physician shall evaluate the individual's capacity and, if the physician concludes that the individual lacks capacity, enter that evaluation in the individual's medical record. If the primary or attending physician has a question as to whether the individual lacks capacity, another physician shall also evaluate the individual's capacity, and if the second physician agrees that the individual lacks the capacity to make health care decisions or provide informed consent, the health care facility shall enter both physicians' evaluations in the individual's medical record. A determination made pursuant to this section that an individual lacks capacity to make health care decisions shall not be construed as a finding that the individual lacks capacity for any other purpose. The MGS IRB applies this law when determining the requirement for signature of a legally authorized representative. Please also see HRP-417 - CHECKLIST - Cognitively Impaired Adults.

Genetic Testing; Informed Consent; Confidentiality; Penalties; Notice of Use of Results (Florida Statutes §760.40)

This law provides that informed consent must always be obtained prior to DNA testing and certain notice must be provided to the subject. DNA analysis means the medical and biological examination and analysis of a person to identify the presence and composition of genes in that person's body. The term includes DNA typing and genetic testing. DNA analysis may be performed only with the informed consent of the person to be tested. The results of such DNA analysis, whether held by a public or private entity, are the exclusive property of the person tested, are confidential, and may not be disclosed without the consent of the person tested, except as specified by statute. A person who performs DNA analysis or receives records, results, or findings of DNA analysis must provide the person tested with notice that the analysis was performed or that the information was received. The notice must state that, upon the request of the person tested, the information will be made available to his or her physician. The notice must

also state whether the information was used in any decision to grant or deny any insurance, employment, mortgage, loan, credit, or educational opportunity. If the information was used in any decision that resulted in a denial, the analysis must be repeated to verify the accuracy of the first analysis, and if the first analysis is found to be inaccurate, the denial must be reviewed.

Protecting DNA Privacy Act (Florida Statutes §§ 760.40; 817.5644)

The State of Florida privacy regulations of the Protecting DNA Privacy Act prohibit the collection, retention, analysis and disclosure of analysis results of a person's DNA sample without express consent for specified purposes. The Protecting DNA Privacy Act is applicable only to a DNA sample collected from a person in Florida, and to the use, retention, maintenance and disclosure of such person's DNA sample or the results of a DNA analysis after the effective date of October 1, 2021.

Investigators conducting research involving optional DNA analysis must use the template Protecting DNA Privacy Act language available in the HRP-502a - Biomedical Adult Consent.

Refer to the "Florida DNA Privacy Act" guidance document located in the Regulation and Guidance section of the MGS IRB homepage.

Sexually Transmissible Disease; Reporting Required (Florida Statutes §384.25)

This law provides that any person who diagnoses or treats a person with a sexually transmissible disease (i.e. in the course of screening for human research eligibility) must report the facts as required by the Department of Health, within the time period specified in 64D-3.029, F.A.C.

Child abuse should be considered by a practitioner upon collection of a specimen for laboratory testing in any person 12 years of age or under, excluding neonates. Reporting of an STD case to a county health department does not relieve the practitioner of their mandatory reporting responsibilities regarding child abuse pursuant to Section 39.201, F.S.

Reporting Requirements for Practitioners and Hospitals for Sexually Transmissible Diseases (STDs) Including HIV and AIDS. Florida Administrative Code Rule 64D-3.029

Pursuant to 64D-3.029, F.A.C. diseases or conditions that are of public health significance identified in 64D-3.029, F.A.C. must be reported in the timeframe and manner specified in 64D-3.029, F.A.C.

Florida Patient's Bill of Rights and Responsibilities (Florida Statutes §381.026(4)(e))

Generally, the statute states that a patient has the right to know if any part of his or her medical treatment is for purposes of experimental research and to consent prior to participation in such research. A patient's participation must be a voluntary matter; and a patient has the right to refuse to participate. The patient's consent or refusal must be documented in the patient's care record.

Rights of Persons Determined Incapacitated (Florida Statutes §744.3215(4)(b))

This law provides that a court-appointed guardian may not consent to participation by the ward in any biomedical or behavioral experiment without the specific authority of the court. A guardian may only consent to enroll a ward in a biomedical or behavioral experiment with the specific authority of the court. The court may only grant such specific authority where participation in the research is of direct benefit to, and is intended to preserve the life of or prevent serious impairment to the mental or physical health of the ward or is intended to assist the ward to develop or regain his or her abilities.

Personal Treatment of Persons Who Are Developmentally Disabled (Florida Statutes §393.13(4)(c)(6))

This law requires that consent be given by a developmentally disabled person or the person's legal guardian prior to instituting a plan of experimental medical treatment. Prior to instituting a plan of experimental medical treatment, express and informed consent shall be obtained from a developmentally disabled individual, if competent, or the individual's parent or legal guardian. Information upon which the individual shall make the decision to participate shall include, but should not be limited to, the nature and consequence of such procedures, the risks, benefits, and purposes of such procedures, and available alternate procedures.

Anatomical Donation (Florida Statutes §§765.512, 756.513 and 765.514)

Research subjects may indicate their intent to make an anatomical gift for research in a document other than a will (i.e. in a consent document), so long as the consent is signed by both the donor and by two witnesses in the donor's presence. If the donor/subject did not provide consent to make an anatomical gift and expires or loses the capacity to consent, persons enumerated in 765.512(3) may, in the absence of any actual notice of contrary indications by the donor/subject or notice of opposition by a prior class, provide consent to give all or part of the donor/subject's body for any purpose specified in 765.513.

Confidentiality of Reports and Records (Florida Statutes §415.107)

This law provides that records concerning reports of abuse, neglect, or exploitation of the vulnerable adult, including reports made to the central abuse hotline, and all records generated as a result of such reports are confidential; however, access to all records, excluding the name of the reporter, may be granted for bona fide human research. Information may be released to persons conducting bona fide research or auditing. However, information identifying the subjects of the report must not be made available to such researchers.

Florida Sunshine and Public Records Law (Florida Statutes §§286.011; 286.012)

This law allows open access to all official meetings and official records maintained by MGS, including IRB meetings and records. There are specific exemptions that apply to certain

meetings and documents. Florida's public meetings law requires that meetings of the IRB and other compliance committees where final decisions are made be open to the public at all times (i.e. that anyone may attend the meeting or any portion thereof), reasonable notice must be provided of the meeting, and minutes must be taken. The law also requires that two or more board members may not discuss a matter outside of the meeting on which foreseeable action will take place at the board meeting. The public meetings law also prohibits members from abstaining from a vote unless there is, or appears to be, a conflict of interest as defined by the Florida Code of Ethics for Public Officers and Employees (Florida Statutes §112.313). However, where federal law requires a member to vote, the state law pertaining to abstaining from votes will be superseded. Federal guidance issued by OHRP recommends that, except when requested by the IRB to be present to provide information, IRB members absent themselves from the meeting room when the IRB discusses and votes on human research with which they have a conflicting interest. Regarding the requirement that the meeting be open to the public at all times, the MGS General Counsel has advised the IRB to treat the federal policy as superseding the public meetings law. Therefore, members with conflicting interests are asked to leave the room temporarily during the public meeting while issues pertaining to the proposal are discussed by the IRB.

Sovereign Immunity (Florida Statutes §768.28)

This law provides for sovereign immunity for the State of Florida and its agencies, including state universities. Sovereign immunity protects individuals who are acting as agents of the graduate school from tort liability exceeding the sum of $200,000 per claim and $300,000 per incident.

International Cultural Agreements (Florida Statutes §768.28)

This law outlines requirements for participating in partnerships, agreements, or receiving grants from Foreign Countries of Concern (FCOC). The statute specifies that any state graduate school authorized to expend state-appropriated funds may not accept any grant from or participate in any partnership with any foreign principal based in a foreign country of concern without the approval of the Board of Governors. Investigators may choose whether to pursue the project by getting approval first from the Board of Trustees and then from the Board of Governors.

Consent on Behalf of Children (referenced as minors in Florida law) to Participate in Medical or Behavioral Research

A child/minor is an individual under the age of 18 whose disabilities have not been removed by marriage or by an act of the court. (Florida Statutes §743.01; §743.015; §743.07; §744.102(13)). Minors are generally presumed to be legally incompetent to consent to medical or mental health treatment. Parents are the minor's natural guardians. A natural guardian is a guardian who can exercise all the legal rights and powers for the minor/ward that can be delegated. (Florida Statutes §744.301). Since a parent/natural guardian can exercise all of a minor's legal rights and

powers, a parent/natural guardian can consent to a minor's participation in experimental research.

In the absence of a natural guardian due to death, incapacity, removal of parental rights or other permanent absence, a minor will normally have a court-appointed guardian or will be a ward of the state. A guardian of a minor may be a permanent guardian or a plenary guardian. A plenary guardian is usually a temporary guardian who is authorized to exercise all the legal rights and powers for the minor that can be delegated. However, unless specifically authorized by the court, a temporary guardian cannot provide legally effective consent to allow a minor's participation in research or experimental treatment. (Florida Statutes §744.3215(4)(b); §744.3725). Unlike a natural guardian or a permanent guardian, a court-appointed plenary guardian of a minor may not consent to the participation of the minor in research without the specific authority of the court. (Florida Statutes §744.3215(4)(b)).

Parental consent is not required for the termination of a pregnancy of a minor; however, actual notice, notice that is given directly, in person or by telephone, must be provided to a parent or legal guardian of a minor, by a physician, at least 48 hours before the inducement or performance of a termination of pregnancy, and documentation must be made in the minor's files. If actual notice is not possible after a reasonable effort has been made, the physician performing or inducing the termination of pregnancy or the referring physician must give constructive notice or notice in writing, signed by the physician, and mailed at least 72 hours before the inducement or performance of the termination of pregnancy, to the last known address of the parent or legal guardian of the minor, by first-class mail and by certified mail, return receipt requested, and delivery restricted to the parent or legal guardian. After the 72 hours have passed, delivery is deemed to have occurred. The notice requirement may be waived under certain circumstances. (Florida Statutes §390.01114).

An unwed pregnant minor may consent to medical or surgical care or services relating to her pregnancy by a hospital, clinic or physician licensed in the state of Florida, and her consent is valid and binding as if she had achieved the age of majority. (Florida Statutes §743.065).

Lotteries are Prohibited (Florida Statutes §§849.09(1)(c); 849.0935(4) (a) (b))

This law states that it is unlawful for any person in this state to conduct a lottery drawing for the distribution of a prize or prizes by lot or chance or advertise any such lottery scheme or device in any newspaper or by circulars, posters, pamphlets, radio, telegraph, telephone, or otherwise. It is thus unlawful for researchers to use a random drawing of chance as a mechanism for compensating research subjects.

Mandatory reports of child abuse, abandonment, or neglect; mandatory reports of death; central abuse hotline (Florida Statutes §39.201)

The law states that any person who knows, or has reasonable cause to suspect, that a child is abused, abandoned, or neglected by a parent, legal custodian, caregiver, or other person responsible for the child's welfare, as defined in this chapter, or that a child is in need of supervision and care and has no parent, legal custodian, or responsible adult relative immediately known and available to provide supervision and care shall report such knowledge or suspicion to the Florida Department of Children and Families by means of the central abuse hotline.

Any person who knows, or who has reasonable cause to suspect, that a child is abused by an adult other than a parent, legal custodian, caregiver, or other person responsible for the child's welfare, as defined in this chapter, shall report such knowledge or suspicion to the Florida Department of Children and Families in the manner prescribed in subsection two (2) of the statute.

Any person who knows, or has reasonable cause to suspect, that a child is the victim of childhood sexual abuse or the victim of a known or suspected juvenile sexual offender, as defined in this chapter, shall report such knowledge or suspicion to the Florida Department of Children and Families in the manner prescribed in subsection two (2) of the statute.

Reporters in the following occupation categories are required to provide their names to the hotline staff:

1. Physician, osteopathic physician, medical examiner, chiropractic physician, nurse, or hospital personnel engaged in the admission, examination, care, or treatment of persons;
2. Health or mental health professionals other than those listed in subparagraph 1;
3. Practitioners who rely solely on spiritual means for healing;
4. School teachers or other school officials or personnel;
5. Social workers, day care center workers, or other professional child care, foster care, residential, or this institution's workers;
6. Law enforcement officers; or
7. Judges.

Areas Where State and Federal Laws Differ

HRPP policies do not specifically identify where state and federal laws differ. Rather, the policies are drafted to incorporate the appropriate action required by the controlling law. Regarding most topics of importance to the HRPP, the federal law provides either broad guidance, or guidance specific to a particular area that state law may or may not address. The state law provides more specific guidance within the broad guidance provided by federal law; the two laws are read to be complementary and in such a way as not to defeat the purpose of either law.

There is only one instance applicable to the HRPP where state law and federal law have incompatible interpretations, according to the MGS General Counsel. Florida's Sunshine law

requires that meetings of the IRB and other compliance committees, where final decisions are made, be open to the public at all times (i.e. that anyone may attend the meeting or any portion thereof). However, the federal policy guidance, issued by OHRP, recommends that, except when requested by the IRB to be present to provide information, IRB members absent themselves from the meeting room when the IRB discusses and votes on human subjects research in which they have a conflicting interest. Although this policy is presented as a "recommendation" by the federal agency, The MGS General Counsel has advised the IRB to treat the federal policy as superseding the Florida Sunshine law. Therefore, members with conflicting interest are asked to leave the room temporarily during the public meeting while issues pertaining to the proposal are discussed by the IRB.

18. What if I want to conduct research in schools or obtain student records?

Studies involving children in primary and secondary educational settings require documentation of approval from the school district/administrator and parental permission unless waived by the IRB. The IRB will require a copy of the district(s) approval letter prior to the commencement of research activities.

Research involving children in schools or student education records require adherence to the Family Educational Rights and Privacy Act (FERPA) 34 CFR 99 and The Protection of Pupil Rights Amendment (PPRA) 20 U.S.C. §1232h; 34 CFR 98.

Family Educational Rights and Privacy Act (FERPA)

FERPA 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 (ED). FERPA applies when researchers obtain student records or personal education information from an education program.

FERPA gives parents certain rights with respect to their children's education records. These rights transfer to the student when he or she reaches the age of 18 or attends a school beyond the high school level. Students to whom the rights have transferred are "eligible students." Generally, schools must have written permission from the parent or eligible student in order to release any information from a student's education record. Schools may disclose without consent "directory" information such as a student's name, address, telephone number, date and place of birth, honors and awards, and dates of attendance.

Education records include a range of information about a student that is maintained in schools in any recorded way, such as handwriting, print, computer media, video or audio tape, film, microfilm, and microfiche. Examples of education records protected under FERPA include: Grades and transcripts; Student schedules; Papers, theses; and other graded coursework; Special education records; Disciplinary records; Medical and health records that the school creates or collects and maintains; Documentation of attendance, schools attended, courses taken, awards conferred, and degrees earned; Advising records; and any personally identifiable information

such as student's identification code, social security number, student email, picture, or other information that would make it easy to identify or locate a student.

Personal notes made by teachers and other school officials that are not shared with others are not considered education records. Additionally, law enforcement records created and maintained by a school or district's law enforcement unit are not education records.

An educational agency or institution may disclose personally identifiable information from an education record of a student without consent if the disclosure is to organizations conducting studies for, or on behalf of, educational agencies or institutions to develop, validate, or administer predictive tests, administer student aid programs, or to improve instruction. A school district or postsecondary institution that uses this exception is required to enter into a written agreement with the Organization or researcher conducting the research. Education records may also be released without consent under FERPA if all personally identifiable information has been removed. For more information on FERPA exceptions and requirements please see, HRP-331 - WORKSHEET - FERPA Compliance.

Protection of Pupil Rights Amendment (PPRA)

PPRA provides parents or guardians with some oversight of the content of third-party research and any instructional materials developed by researchers. PPRA identifies “sensitive topics” and “provisions for parental review and approval” for surveys and materials. PPRA applies to programs that receive funding from the ED and is intended to protect the rights of parents and students in two ways:

1. It seeks to ensure that schools and contractors make instructional materials available for inspection by parents or guardians if those materials will be used in connection with an ED-funded survey, analysis, or evaluation in which their children participate; and
2. No student shall be required, as part of any research project, to submit without prior consent to surveys, psychiatric or psychological examination, testing, or treatment, in which the primary purpose is to reveal information concerning one or more of the following:
    - Political affiliations or beliefs of the student or student’s parents;
    - Mental and psychological problems of the student and his/her family;
    - Sex behavior and attitudes;
    - Illegal, anti-social, self-incriminating, and demeaning behavior;
    - Critical appraisals of other individuals with whom respondents have close family relationships;
    - Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers;
    - Religious practices, affiliations or beliefs of the students or the student’s parents; or
    - Income other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program.

Schools and contractors must obtain prior written parental consent before minor students are required to participate in any ED-funded survey, analysis, or evaluation.

19. What if I want to include deception in my research?

While the use of deception may be a valuable methodology to avoid bias or test a hypothesis, these techniques raise important ethical issues. The federal regulations for obtaining informed consent require full disclosure of the research to the subject and therefore, the IRB must determine the extent to which the deception interferes with the subject's ability to provide fully informed consent.

Deception involves misleading subjects as to the true nature of the study procedures. Deception includes both active deception and deceptive incomplete disclosure:

- Active deception is a situation where an individual is provided false or misleading information regarding the true purpose of the study. Examples of active deception include providing a "cover story" which falsely describes the purpose of the research or using a "confederate" or study accomplice who is posing as a research subject whose behavior in the study is actually part of the research design.
- Deceptive incomplete disclosure is a situation in which an investigator withholds information about the specific purpose, nature, or other aspect of the research; and 1) that information, if provided during initial consent may have affected subjects' decisions to participate and/or 2) when subjects learn of the information withheld, they would likely feel deceived. An example of deceptive incomplete disclosure includes audiotaping or videotaping subjects without their knowledge or consent.

Not all incomplete disclosure is considered deception. An example of non-deceptive incomplete disclosure includes not revealing the hypotheses of the study. The researcher may provide information to the subject about the research that is true, yet not detailed enough to reveal the main aims or hypotheses of the study. In most cases, this would not be considered deception.

The use of deception must be justified and there should be no reasonable alternative method that would be equally effective. To approve research involving deception, the study procedures cannot involve greater than minimal risk to subjects.

The Investigator must clearly outline that the proposed research involves deception in their initial application to the IRB. The Investigator must provide a script to be used during the debriefing session after the subject's participation in the research study and utilize this to debrief subjects unless the IRB determines that such debriefing would cause harm to the subject. After debriefing, the Investigator must ask subjects if they would like their study information withdrawn and withdraw the study information should this be requested by the subject.

The IRB Chair, or Vice Chair reviews applications for initial review. Studies involving deception can be reviewed by expedited procedures depending on the risks to subjects and level of

deception used in the research. Research involving deception does not qualify for review by exempt procedures, except for research that meets the criteria for approval under 45 CFR 46.104(d)(3). In this case, deception while conducting benign behavioral interventions can only be used if the subject prospectively agrees to the use of deception. Subjects must be informed prior to initiating the intervention that they will be unaware of or misled regarding the true nature or purpose of the research. They will also be told whether further information will be provided at the conclusion of the research activities. Researchers should still debrief subjects.

20. How do I create a consent document?

Use the HRP-502x - TEMPLATE CONSENT DOCUMENT to create a consent document. The currently available templates are:

- HRP-502a - Biomedical Adult Consent
- HRP-502a(1) - Biomedical Adult Spanish Consent
- HRP-502a(2) - Biomedical Assent
- HRP-502a(3) - Biomedical Parental Permission
- HRP-502a(4) - Biomedical LAR
- HRP-502b - Social Behavioral Adult Consent
- HRP-502b(1) - Social Behavioral Adult Spanish Consent
- HRP-502b(2) - Social Behavioral Assent
- HRP-502b(3) - Social Behavioral Parental Permission
- HRP-502b(5) - Social Behavioral Combined Consent and Parental Permission
- HRP-502b(6) - Social Behavioral Proxy (LAR) Consent
- HRP-502b(7) - Social Behavioral Survey, Interview, and Focus Group Consent (No Signature)
- HRP-502c - Genetic/Genomic Consent Addendum
- HRP-506 - Expanded Access/Compassionate Use Consent

Note that all consent documents must contain all of the required and all additional appropriate elements of informed consent. Review the “Elements of Consent Disclosure” section #7 in the IRB’s HRP-314 - WORKSHEET - Criteria for Approval, to ensure that these elements are addressed. See also HRP-090 - SOP - Informed Consent Process and HRP-091 - SOP - Written Documentation of Consent for additional special considerations related to the consent process. The consent templates include required language for MGS research. MGS will not allow the use of broad consent pending additional guidance on the topic from OHRP. The IRB will not approve language in the informed consent document which may be exculpatory, in which subjects (or their legally authorized representatives) are made to waive or appear to waive any legal rights or release the Investigator, sponsors, or institution from liability for negligence. MGS investigators conducting research involving Protected Health Information (PHI) must use the

MGS HIPAA authorization language available in the HRP-502a - Biomedical Adult Consent. See Question 32 for use of electronic signatures when consenting subjects.

Transfer of subject from a study site to MGS

For research subjects that are transferred to a MGS or MGS affiliate site from another study site, the MGS or MGS affiliate site receiving the subject must have subject(s) sign an updated MGS IRB-approved consent upon enrollment at the new site with local updated contact information and institutionally required language.

Non-English Speaking Human Subjects

When recruiting subjects whose primary language is not English, these individuals must be consented and provided with an informed consent document in their native language. An individual who speaks the same language as the subject must be included in the consent process to translate questions or concerns between the subject and the individual obtaining consent. The translator does not need to be a member of the study team but must be able to communicate accurately and honestly between the subject and the research team. In addition, the MGS IRB recommends that the translator not be a family member of the potential research subject. Once the IRB has reviewed and approved the English version of the informed consent document, the approved document must be translated into the language understandable by potential subjects and submitted as a Modification for IRB approval. The translated copy may be submitted with the English consent form with the initial submission as an alternative to submitting a Modification; however, changes requested to the English version must also be reflected in the non-English version. The translated document must be certified by a licensed translator or translation company, or back-translated. The certification must attest that the translation is accurate and complete. Back-translated documents should be translated by an individual who speaks the language fluently, and back-translated by a different, non-study team member who speaks the language fluently. Major discrepancies with the English version must be addressed.

Informed Consent and the NIH Genomic Data Sharing (GDS) Policy

For research that falls within the scope of the NIH GDS Policy, the IRB must review the informed consent document to determine whether it is appropriate for data to be shared for secondary research use. Investigators must obtain prospective consent for the use of genomic and phenotypic data to be used in future research and to be shared broadly. In addition, the informed consent document should include whether the subject's data will be shared through unrestricted or controlled access repositories even though the data are submitted de-identified. Investigators need to clearly define the subject population because genomic research in identifiable populations (i.e., specific racial or ethnic groups, geographically defined communities and members of ultra-rare disease groups) presents unique privacy concerns.

21. Do I need to include injury language in my consent?

For research that involves greater than minimal risk, the IRB reviews and approves language in the informed consent document related to compensation and treatment for research related injuries. Injury includes physical injury, as well as psychological or social harm, or harm to one's dignity, depending on the nature of the research. MGS investigators conducting research involving more than minimal risk to subjects must use the MGS subject injury language available in the HRP-502a - Biomedical Adult Consent. This language is to be included in all greater than minimal risk consents regardless of who is funding the research or acting as the IRB of record. If the sponsor of the research is private industry, the same language must be included within any contract or agreement the graduate school has with them for consistency. No changes to this language can occur without the sign off from the MGS IRB. If a sponsor is requesting changes to this language, please reach out the IRB Office at IRB@mgsns.org

22. Can I compensate subjects for their participation?

The IRB reviews the amount and method of compensation to research subjects and the proposed payment schedule to ensure the compensation does not present undue influence (an offer of an excessive or inappropriate reward or other overture in order to obtain compliance) to individuals participating in IRB approved research. Compensation should only be offered in accordance with the following:

- Compensation should not be contingent upon the subject completing the study, but should accrue as the study progresses.
- Compensation given as a "bonus" or incentive for completing the study is acceptable provided that the amount is not coercive. The IRB will make the final determination whether the amount is not so large as to be coercive or represent undue influence.
- Pursuant to Florida law (Florida Statute 456.054), the IRB does not allow payments designed to accelerate recruitment (also known as bonus payments) or allow referrals that result in a "finder's fee" payment.
- Compensation should be based on the time an individual will be involved with study procedures, the inconvenience or discomfort to the subject, and reimbursement for expenses incurred while participating.
- Compensation should be equal for all subjects who participate with equal time and effort in the study.
- Compensation methods and amounts should be considered based on the target study population, cultural aspects, country of residence, and other relevant information.
- Pursuant to Florida law (Florida Statute 849.09(1)(c)), a random drawing for monetary or other awards cannot be used as an incentive for enrolling or continuing participation in human subjects research.

Compensation is not viewed as a benefit to participation in research and should not be outlined as such in the informed consent document or considered by the IRB in the assessment of the

risks and benefits to subjects. Sponsor coupons for a discount on the purchase price of the product once it has been approved for marketing is prohibited as compensation for participation.

Finally, investigators are responsible for collecting taxpayer information from research subjects in accordance with MGS Research Clarification or Change in Procedure (CCHIP) #017. Check with your department's fiscal contact to make sure that you are following your respective college's policies (e.g. use of payment apps, gift cards, etc.).

If extra credit or rewards are offered for participation, students must be provided with and informed of non-research alternatives involving comparable time and effort to obtain the extra credit in order for the possibility of undue influence to be minimized.

23. What are the different regulatory classifications that research activities may fall under?

Submitted activities may fall under one of the following four regulatory classifications:

- Not Human Subjects Research: Activities must meet the institutional definition of human subjects research to fall under IRB oversight. Activities that do not meet this definition are not subject to IRB oversight or review. Review the HRP-310 - WORKSHEET: Human Subjects Research Determination for reference. Contact the IRB in cases where it is unclear whether an activity is human subjects research.
- Exempt: Certain categories of human subjects research may be exempt from regulation but require IRB review. It is the responsibility of the IRB, not the Investigator, to determine whether human subjects research is exempt from IRB review. Review the HRP-312 – WORKSHEET- Exemption for reference on the categories of research that may be exempt.
- Review Using the Expedited Procedure: Certain categories of non-exempt human subjects research may qualify for review using the expedited procedure, meaning that the project may be approved by a single designated IRB reviewer, rather than the convened board. Review the HRP-313 - WORKSHEET - Expedited Review for reference on the categories of research that may be reviewed using the expedited procedure.
- Review by the Convened IRB: Non-Exempt human subjects research that does not qualify for review using the expedited procedure must be reviewed by the convened IRB.

24. What are the decisions the IRB can make when reviewing proposed research?

The IRB may approve research, require modifications to the research to secure approval, table research, defer research or disapprove research:

- Approval: Made when all criteria for approval are met. See Question #25 of this Investigator Manual.
- Modifications Required to Secure Approval: Made when IRB members require specific modifications to the research before approval can be finalized.

- Tabled: Made when the IRB cannot approve the research at a meeting for reasons unrelated to the research, such as loss of quorum. When taking this action, the IRB automatically schedules the research for review at the next meeting.
- Deferred: Made when the IRB determines that the research cannot be approved without substantive changes to the protocol or informed consent form, the IRB suggests modifications that might make the research approvable. When making this motion, the IRB describes its reasons for this decision, describes modifications that might make the research approvable, and gives the Investigator an opportunity to respond to the IRB in writing. Research that is deferred must be reviewed again at a fully convened IRB meeting.
- Disapproval: Made when the IRB determines that the research is not approvable because it does not meet the criteria for IRB approval found in 45 CFR 46.111/21 CFR 56.111. When making this motion, the IRB describes its reasons for this decision and gives the Investigator an opportunity to respond to the IRB in writing.

25. How does the IRB decide whether to approve human subjects research?

The criteria for IRB approval can be found in the HRP-312 – WORKSHEET- Exemption for exempt human subjects research and the HRP-314 - WORKSHEET - Criteria for Approval for non-exempt human subjects research. The latter worksheet references other checklists that might be relevant. All checklists and worksheets can be found in the MGS IRB Library. These checklists follow the 45 CFR 46.111/21 CFR 56.111 requirements.

These checklists are used for initial review, continuing review, and review of modifications to previously approved human subjects research.

You are encouraged to use the checklists to write your Investigator Protocol in a way that addresses the criteria for approval.

26. What will happen after IRB review?

The IRB will provide you with a written decision indicating that the IRB has approved the human subjects research, requires substantive or non-substantive modifications to secure approval, or has disapproved the human subjects research.

- If the IRB has approved the human subjects research: The human subjects research may commence once all other institutional approvals have been obtained. IRB approval is usually good for a limited period of time, which is noted in the approval letter. Approval letters may also have special instructions from the IRB.
- If the IRB requires modifications to secure approval: All required changes will be outlined in a letter. Make the requested modifications and submit them to the IRB. If all requested modifications are made, the IRB will issue a final approval. If you do not agree with the modifications, write up your response with justification as to why the modifications cannot/should not be made and submit it to the IRB. If a response or

request for an extension is not received by close of business on the thirtieth (30th) calendar day from receipt of the letter requesting modifications, the IRB will close the application. For continuing review applications, if a response is not received by close of business on the tenth (10th) calendar day from the date of expiration, IRB approval will lapse and the study will be suspended.

- If the IRB defers the human subjects research: The IRB will provide a statement of the reasons for deferral and suggestions to make the study approvable, and give you an opportunity to respond in writing. In most cases, if the IRB's reasons for the deferral are addressed, the human subjects research can be approved. If a response or request for an extension is not received by close of business on the sixtieth (60th) calendar day from receipt of the letter stating the reasons for deferral and suggested changes, the IRB will close the application.
- If the IRB disapproves the human subjects research: The IRB will provide a statement of the reasons for disapproval and give you an opportunity to respond in writing.
    - If the Investigator believes the decision of the IRB is unduly restrictive, the Investigator may contact the Chairperson, Chair Designee, or IRB administration to discuss the reasons for the determination. The Investigator may appeal the decision of the IRB in writing within thirty (30) calendar days of receiving notice of the determination. Extension to the deadline must be reviewed and approved by the IRB Chairperson. Appeals must be addressed to the IRB Chairperson or Chair Designee and include the reasons the Investigator believes the proposed research or issue at hand follows IRB policies and procedures, state and local laws, and federal regulations. The IRB will consider the appeal(s) based upon new information provided. The Investigator may attend the IRB meeting(s) where his/her research and appeal are reviewed to address issues raised by the convened IRB consistent with MGS Research Integrity & Compliance Procedures for Appearances before Institutional Compliance Committees which can be found on Research Integrity & Compliance website under meeting schedules.

27. What are my obligations after MGS IRB approval?

Investigator obligations when MGS is the IRB of record (i.e., the Reviewing IRB) are numerous depending on the complexity and risk of the study. Keep in mind that obligations for Investigators leading a single IRB study are located under Question #29 of this Investigator Manual and those using an external IRB are under Question #30.

Before Research Begins

- Do not start human subjects research activities until you have obtained and read the final IRB approval letter.
- Do not start human subjects research activities until you have obtained all other required institutional approvals, including approvals of departments, divisions, or institutions where the research will be carried out that require approval prior to commencing research that involves their resources.

- Ensure that there are adequate resources to carry out the research safely. This includes but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment, and space.
- Ensure that research staff are qualified (e.g., including but not limited to appropriate training, education, expertise, credentials, protocol requirements, and, when relevant, privileges) to perform procedures and duties assigned to them during the study.
    - For non-exempt research requiring ongoing IRB oversight, obtain IRB approval prior to making any changes to the list of study personnel.
    - Ensure required training are kept current throughout the research.

Ongoing Routine Obligations

- Personally conduct or supervise the human subjects research. Recognize that the Investigator is accountable for the failures of any study team member.
    - Conduct the human subjects research in accordance with the relevant current protocol as approved by the IRB, and in accordance with applicable federal regulations and local laws.
    - When required by the IRB, ensure that consent or permission is obtained in accordance with the relevant current protocol as approved by the IRB. For consent requiring a signature on paper, study teams must utilize the consent with the IRB effective date stamp and watermark. Most IRB-approved electronic signature methods require an IRB stamped and watermarked version to be used but exceptions will be approved on a case-by-case basis if the rationale is written in detail in the protocol. See Question #38 of this Investigator Manual for more information on storing consents. See Question 32 for the use of electronic signatures when consenting subjects.
    - Do not modify any portion of the human subjects research without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to subjects.
    - Protect the rights, safety, and welfare of subjects involved in the research.
- For exempt research, once the exempt determination is made, the application is closed in MGS IRB. This does not limit your ability to conduct the research. Any proposed or anticipated change to the study design that was previously declared exempt from IRB oversight must be submitted to the IRB as a new study prior to initiation of the change. However, administrative changes, including changes in research personnel (excluding a change in PI), do not warrant a modification or new application. If changes are made and there are questions about whether these activities impact the exempt determination, please submit a new request to the IRB for a determination.
- Submit to the IRB:
    - Proposed modifications as described in this manual for expedited and full IRB review applications. (See Question #33 of this Investigator Manual)
    - Personnel Change Requests (PCR) to add/remove study team members.
    - A continuing review application as requested in the approval letter. (See Question #35)
    - A continuing review application when the human subjects research is closed. (See Question #36)

  - Submit an updated disclosure of financial interests within thirty (30) days of discovering or acquiring (e.g. through purchase, marriage, or inheritance) a new financial interest. (See Question #5)
- Do not accept or provide payments to professionals in exchange for referrals of potential subjects (i.e. "finder's fees") as required by law.
- Do not accept payments designed to accelerate recruitment that were tied to the rate or timing of enrollment (i.e. "bonus payments").
- See additional requirements of various federal agencies in Appendix A. These represent additional requirements and do not override the baseline requirements of this section.
  - If the study meets the definition of a clinical trial and supported by a Common Rule agency, one IRB-approved version of a consent form that has been used to enroll subjects must be posted on a public federal website designated for posting such consent forms. The form must be posted after recruitment closes, and no later than sixty (60) days after the last study visit. Please contact the study sponsor with any questions.
  - If certain information should not be made publicly available on a Federal website (e.g. confidential commercial information), the supporting Federal department or agency may permit or require redactions to the information posted. Contact the Federal department or agency supporting the clinical trial for a formal determination.
  - Contact the supporting Federal department or agency sponsor with any other questions regarding consent form posting obligations.
- Refer to Question #39 of this Investigator Manual for information on record keeping and data confidentiality.
- If the Investigator will be leaving the Institution, the Investigator is required to inform the MGS HRPP within 60 days prior to employment end date.
  - Research documents such as consent and identifiable data must remain at MGS.
  - If the Investigator is planning to continue their research at another institution they must provide a plan for transferring IRB oversight to their new institution, including how/what data will be transferred.
  - Prior to leaving the Institution, the Investigator is responsible for either closing out the study (see Question #37 of this Investigator Manual) or submitting a Modification application to change oversight to a new MGS Investigator who is eligible to serve as a PI.

Reporting Unforeseen Events

- Complete the Reportable New Information (similar to the previous "Reportable Event") within <u>five (5) business days</u> of being notified of the information for any of the following items:
  - Information that indicates a new or increased risk, or a new safety issue. For example:
    i) New information (e.g. an interim analysis, safety monitoring report, publication in the literature, sponsor report, or Investigator finding) indicates an increase in the frequency or magnitude of a previously known risk, or uncovers a new risk.
    ii) An Investigator's Brochure, package insert, or device labeling is revised to indicate an increase in the frequency or magnitude of a previously known risk, or describe a new risk.

iii) Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol.
iv) Protocol violation that harmed subjects or others or that indicates subjects or others might be at increased risk of harm.
v) Complaint from a subject that indicates subjects or others might be at increased risk of harm or at risk of a new harm.
vi) Any changes significantly affecting the conduct of the research that may increase risk.

- Harm experienced by a subject or other individual, which in the opinion of the Investigator are **unexpected** and **probably related** to the research procedures.
  i) A harm is "unexpected" when its specificity or severity are inconsistent with risk information previously reviewed and approved by the IRB in terms of nature, severity, frequency, or characteristics of the study population.
  ii) A harm is "probably related" to the research procedures if in the opinion of the Investigator, the research procedures more likely than not caused the harm.
- Serious or continuing non-compliance with the federal regulations governing human subjects research or with the requirements, policies, or determinations of the IRB, or an allegation of such non-compliance.
  - For Department of Veterans Affairs (VA) research, local deaths, unanticipated SAEs, or apparently serious research information security problems.
- Audit, inspection, or inquiry by a federal agency.
  - Include any resulting reports with your responses. This should be reported to the IRB regardless of the reason for the inspection. Ideally, the Investigator should notify the IRB prior to the inspection.
  - For-cause inspections or audits by sponsors and any resulting communication and/or report.
- Breach of confidentiality or possible breach by way of compromised data access (e.g. lost consent, stolen computer or misplaced records).
- Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject.
- Premature suspension, termination, or hold of the research by the sponsor, Investigator, institution, or oversight body (e.g. DSMB or FDA) for any reason.
- Unanticipated adverse device effect (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).

- Complete the Reportable New Information Form (similar to the previous "Reportable Event") within thirty (30) business days of being notified of the information for any of the following items:
  - Non-serious or non-continuing non-compliance with the federal regulations governing human subjects research or with the requirements, policies, or determinations of the IRB, or an allegation of such non-compliance.

    - Failure to follow the protocol regarding safety procedures due to the action or inaction of the Investigator or research staff.
    - An exception from the IRB approved protocol that has been approved by the sponsor of the research.
    - Complaint from a subject that cannot be easily resolved by the research team.
  - Provide at continuing review or via an RNI at the yearly check in:
    - Written reports from study monitors to be submitted as required by the sponsor and/or sponsor's agent, or Data and Safety Monitoring Board (DSMB) reports.
    - Failure to follow the protocol regarding due to the action or inaction of the Investigator or research staff.
- Complete the Reportable New Information (RNI) Form to report negative findings by a government oversight office, legal action related to human research protections, or unfavorable media coverage within twenty-four (24) hours of learning of the findings or event. This includes:
  - Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA restrictions placed on IRBs or Investigators, and corresponding compliance actions taken under non-US authorities related to human subjects research protections.
  - Any litigation, arbitration, or settlements initiated related to human research protections.
  - Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding MGS's HRPP.

28. What are some examples of adverse events (AEs) and serious adverse events (SAEs) that need to be submitted within five (5) business days of becoming aware of the event?

Interventional Biomedical Research:

- A single occurrence of a serious, unexpected event that is uncommon and strongly associated with drug exposure (e.g. severe allergic reaction, acute liver injury, or prolonged bleeding);
- A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with drug exposure, and uncommon in the study population (e.g. tendon rupture, inflammatory brain injury with mild or severe symptoms);
- Multiple occurrences of an AE that, based on aggregate analysis, is determined to be an unanticipated problem. There should be a determination that the series of AEs represents a signal that the AEs were not just isolated occurrences and involve risk to human subjects (e.g. a comparison of rates across treatment groups reveals higher rate in the drug treatment arm versus control arm);
- An AE that is described or addressed in the Investigator's Brochure, protocol, or informed consent documents, but occurs at a frequency or severity that is inconsistent with prior observations. A discussion of the divergence from the expected frequency or severity should accompany the report (e.g. drug known to cause nausea but not known to cause excessive vomiting leading to a trip to the hospital);

- An SAE that is described or addressed in the Investigator's Brochure, protocol, or informed consent documents, but for which the rate of occurrence in the study represents a clinically significant increase in the expected rate of occurrence. A discussion of the divergence from the expected rate should accompany the report (e.g. drug known to cause serious anemia in 2% of subjects but this overall trial and/or site shows the rate at 5%);
- Any other AE or safety finding that would cause the sponsor to modify the Investigator's Brochure, study protocol, or informed consent documents, or would prompt other action by the IRB to ensure the protection of human subjects. It is recommended that an explanation of the conclusion accompany the report;
- Any change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol;

Interventional Biomedical or Social Behavioral Research:

- Any behavioral intervention that triggers a serious physical or mental health condition (e.g. underlying depression escalates to suicidal actions, PTSD worsens to create violent acts against self or others);
- Any change to the protocol that was taken without prior IRB approval to eliminate apparent immediate hazard to a research subject;
- Though not considered an AE, the IRB still needs to be notified of the following:
    - Incarceration of a subject when enrolled on a study not approved under Subpart C provisions; or
    - Breach of privacy or confidentiality that would place the subject or others at risk including the loss of data on a computer or any electronic device which holds private or confidential information.

29. *What are my obligations as the overall study Investigator for a single IRB (sIRB) study?*

- Coordinating with IRB Reliance Manager to determine whether this institution's IRB can act as the IRB for all or some institutions participating in the study or if an external IRB will assume oversight. See also Question #8 and Question #9 of this Investigator Manual;
- Identifying whether any IRB fees will be charged for this study and address any budget considerations.
- Identifying all sites that will be engaged in the human subjects' research and requiring oversight by the IRB;
- Ensuring that all sites receive a request to rely on the Reviewing IRB (MGS IRB) and that all institutional requirements are satisfied before a study is activated at a relying site (HRP-817 - FORM - Local Context Questionnaire);
- Collaborating with the Reviewing IRB to document roles and responsibilities for communicating and coordinating key information from study teams and the IRB or HRPP at relying sites (HRP-830 - WORKSHEET - Communication and Responsibilities);
- Responding to questions or information requests from study teams or the IRB or HRPP staff at relying sites;
- Providing relying site investigators with the policies of the Reviewing IRB;

- Providing relying site investigators with the IRB-approved versions of all study documents, including approved consent forms;
- Preparing and submitting IRB applications on behalf of all sites. This includes initial review, modifications, personnel updates, reportable new information, and continuing review information for all sites;
- Establishing a process for obtaining and collating information from all sites and submitting this information to the Reviewing IRB. This includes site-specific variations in study conduct, such as the local consent process and language, subject identification and recruitment processes, and local variations in study conduct (HRP-508 - Biomedical Site Supplement Protocol Template or HRP-508a - Social-Behavioral Site Supplement Protocol Template). See Question #32 for how to consent using an electronic signature;
- Ensuring that consent forms used by relying sites follow the consent template approved by the Reviewing IRB and include required language as specified by the relying sites;
- Providing site investigators with all determinations and communications from the Reviewing IRB (HRP-817 - FORM - Local Context Questionnaire);
- Submitting reportable new information from relying sites to the Reviewing IRB in accordance with the terms outlined in the authorization agreement or communication plan;
- Reporting the absence of continuing review information from relying sites if they do not provide the required information prior to submission of the continuing review materials to the Reviewing IRB. Notifying the relying site of their lapse in approval and applicable corrective actions;
- Providing study records to the relying institution, Reviewing IRB, or regulatory agencies upon request;
- Having a process for monitoring conduct of the research at the participating institution, including but not limited to ensuring all study staff have HSP training and data entered is reviewed for accuracy per your data monitoring plan. These efforts should be documented in the study's regulatory file; and
- See Question #27 of this Investigator Manual for all the ongoing responsibilities of the MGS PI in overseeing both the local and relying sites.

30. What are my obligations as Investigator when relying on an external IRB (Reviewing IRB)?

When an Investigator is required to rely on another IRB by the single IRB mandate or chooses to use an external commercial IRB, they are required to involve the MGS IRB and MGS Research Compliance office. In these situations, the MGS IRB is referred to as the Relying IRB and the external IRB is the Reviewing IRB (also known as the IRB of record). These are the basic obligations to MGS, but this is not an exhaustive list:

- Obtaining appropriate approvals from this Institution prior to seeking review by another IRB;
- Complying with determinations and requirements of the Reviewing IRB;
- Prepare consent and other study documents that are consistent with those approved by the IRB (e.g., use the approved consent template to create site-specific documents);
- Providing the Reviewing IRB with requested information about local requirements or local research context issues relevant to the IRB's determination prior to IRB review;

- Notifying the Reviewing IRB when local policies that impact IRB review are updated;
- Cooperating in the Reviewing IRB's responsibility for initial and continuing review, record keeping and reporting, and providing all information requested by the Reviewing IRB in a timely manner;
- Disclosing conflicts of interest as required by the Reviewing IRB and complying with management plans. See Question #5 of this Investigator Manual;
- Promptly reporting to the Reviewing IRB any proposed changes to the research and not implementing those changes to the research without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subjects;
- Specifying the contact person and providing contact information for researchers and research staff to obtain answers to questions, express concerns, and convey suggestions regarding the use of the Reviewing IRB;
- Fulfill any communication responsibilities as outlined in HRP-830 - WORKSHEET - Communication and Responsibilities;
- Any changes in PI must be submitted and approved to the Reviewing IRB;
- Keeping the approved listed of local research personnel up-to-date within MGS IRB;
- When enrolling subjects, obtain, document and maintain records of consent for each subject or each subject's legally authorized representative;
- In multi-site studies in which a research subject(s) is transferred to MGS from another study site, the MGS site receiving the subject must have the subject(s) sign the IRB approved consent document which contains local contact information and institutionally required language, etc.;
- Maintain research records as noted in Question #38 and Question #39 of this Investigator Manual;
- Promptly reporting to the Reviewing IRB:
    - Any local Unanticipated Problems Involving Risks to Human Subjects or Others according to the requirements specified in the reliance agreement;
    - Any non-compliance, subject complaints, protocol deviations, or other events according to the requirements specified in the reliance agreement;
    - Any data safety monitoring reports in accordance with the Reviewing IRB's reporting policy;
- Complete the Reportable New Information (RNI) Form to report negative findings by a government oversight office, legal action related to human research protections, or unfavorable media coverage within twenty-four (24) hours of learning of the findings or event. This includes:
    - Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA restrictions placed on IRBs or Investigators, and corresponding compliance actions taken under non-US authorities related to human subjects research protections.
    - Any litigation, arbitration, or settlements initiated related to human research protections.

  - Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding MGS.
- Complete the MGS IRB Reportable New Information (RNI) Form (similar to the previous "Reportable Event") within five (5) business days of a determination being made by the Reviewing IRB for any of the following items so that the MGS HRPP can acknowledge the determinations:
  - Information that indicates a new or increased risk, or a new safety issue.
  - Harm experienced by a subject or other individual, which in the opinion of the Investigator are **unexpected** and **probably related** to the research procedures (events that are local).
  - Serious or Continuing non-compliance with the federal regulations governing human subjects research or with the requirements, policies, or determinations of the IRB, or an allegation of such non-compliance.
  - Local breach of confidentiality.
  - Complaint from a subject that cannot be easily resolved by the research team.
  - For-cause inspections or audits by sponsors.
- Yearly provide the MGS IRB with documentation that MGS is still engaged in the research via "Report Continuing Review Data" activity in MGS IRB.
  - If not already done, complete the shell application for studies that migrated from eIRB to MGS IRB.
  - Provide the status of the study e.g., enrolling, active on intervention, follow-up, etc.) and the number of subjects enrolled to date.
  - Provide the current Continuing Review approval letter from the external reviewing IRB.
  - Provide the current Informed Consent Documents approved by the Reviewing IRB.
  - Provide a deviation log that includes:
    i) Failure to follow the protocol regarding due to the action or inaction of the Investigator or research staff.
    ii) Local routine FDA inspection without receipt of an FDA Form 483.
    iii) Non-serious or non-continuing non-compliance with the federal regulations governing human subjects research or with the requirements, policies, or determinations of the IRB, or an allegation of such non-compliance.

31. What do I need to know about recruiting subjects?

Investigators must provide detailed information regarding how subjects will be identified and recruited in the protocol. Recruitment methods and advertisements that will be used in human subjects' research require prospective review and approval by the IRB. There are restrictions on recruiting Student, Employees and Staff as noted below in more detail. The IRB considers advertising or soliciting study subjects to be the start of the informed consent process.

The IRB does not allow "cold calls/approaches" to potential research subjects. A letter of introduction from a direct care provider or organization leader (i.e. someone who has an established relationship with the potential subject) is an acceptable method of disseminating information regarding research opportunities. This information should contain pertinent

information regarding the proposed research and contact information of the study team. Typically, this letter is sent under the name of the individual with whom the potential subject has a direct relationship (i.e. the individual's primary or specialty care provider).

Additionally, a direct care provider may verbally explain the study and if the subject expresses interest, introduce a study team member to discuss the study in more detail.

However, the IRB may not deem these methods of recruitment appropriate for certain research topics, or may approve other methods of recruitment involving calling, emailing, or sending letters depending on the study population.

Please be aware that when detailing the number of individuals that will be recruited/enrolled in the research, the IRB defines enrolled as the number of records reviewed or subjects who agree to participate via a verbal, online, and/or written consent.

Advertisements

Advertisements include printed material and electronic material (e.g. social media posts) that are intended to be seen or audio materials that are intended to be heard by prospective research subjects to solicit and induce prospective research subjects' participation in a study. Advertisements can include printed material and electronic material (e.g. social media posts) that are intended to be seen or audio material that is intended to be heard. Direct advertising includes, but is not necessarily limited to; newspaper, radio, TV, bulletin boards, posters, and flyers that are intended for prospective subjects. This sometimes also includes press releases by the sponsor of the study. Direct advertising does not include communications intended to be seen or heard by health professionals, such as "dear doctor" letters and doctor-to-doctor letters (even when soliciting for study subjects), news stories, or informational publications intended for other audiences. Investigators are responsible for developing advertisement(s) in a non-biased manner without overemphasis of the font size, compensation, or any other items that would unduly influence subjects to participate in the research. Investigators must obtain any necessary approval(s) from sites where the advertisements will be placed (e.g. public transportation, businesses, and schools).

Advertisements should use lay terms and must include the following information:

- The words "Research" or "Research Study;"
- The name of the institution conducting the research & the MGS and/or other appropriate logo;
- The name and contact information of the Investigator conducting the research;
- The condition under study including the purpose of the research;
- Basic criteria used to determine eligibility;
- The IRB study number;
- A brief list of potential benefits to participation (note that compensation for participation is not a benefit to participate in research);
- Time commitment for participation; and

- Compensation or reimbursement (if applicable. Note: the amount should not be overemphasized with bold or enlarged print or other means of emphasis).

Advertisements must not contain:

- Exculpatory language where the subjects would be required to give up some of their rights;
- A promise for a favorable outcome or benefits;
- Promotion for emphasis that subjects will be receiving medical treatment at no cost (free medical treatment) since the reality is that they will not be charged to participate in a research project;
- Explicit or implicit claims of equivalency or superiority to other standards of treatments or safety and efficacy;
- Wording that the study involves "new treatment," "new medication," or "new drug" without an explanation that the treatment is investigational; and
- Claims, explicitly or implicitly, about the drug, biologic or device under investigation that are inconsistent with FDA labeling.

The IRB must review the final copy of printed advertisements to evaluate the font size and other visual effects used and the IRB must also review the final script of audio or video taped advertisements. Advertisement text for television and/or radio broadcasting may be submitted for review and approval prior to the final taping. Investigators should specify in their protocol all advertising formats that are anticipated. Once a study is approved by the IRB, any changes to recruitment and advertising material or methodology must be submitted as a modification and approved prior to use.

Advertisements regarding clinical trials posted on the web (i.e. institutional website or clinicaltrials.gov) do not require prior approval by the IRB as long as the information is limited to basic study details such as:

- The title;
- The purpose of the study;
- The protocol summary;
- Basic eligibility criteria;
- Study site location; and
- Contact information for further information.

Investigators of clinical trials are responsible for registering on clinicaltrials.gov as required by federal regulation. For additional information on registering studies on clinicaltrials.gov, please see the guidance document on the IRB website.

ResearchMatch

A nonprofit program funded by the National Institutes of Health (NIH). It helps to connect people interested in research studies with researchers from top medical centers across the U.S. MGS is participating and has recognized this as a method for recruiting potential subjects.

Researchers would indicate in the protocol that ResearchMatch will be utilized in the table of the Recruitment Methods (Section 13.0 in HRP-503 - Biomedical Protocol Template and 12.0 in HRP-503a - Social Behavioral Protocol Template). Along with the check box, there will need to be a written description included just below the table. If the version of your previously submitted and approved protocol does not contain a box for "ResearchMatch" check the Other box and include ResearchMatch within the information in the protocol.

Along with the changes to the protocol all requests must include the HRP-500 - ResearchMatch and will need to be uploaded into Section 2 of the Local Site Documents page. This document will be stamped once the submission is completed and will need to be given to the ResearchMatch Liaison in order for your project to be listed.

Before listing your project, the ResearchMatch Liaison will verify that your IRB study status is non-expired and that the ResearchMatch campaign is IRB-approved. For any questions/comments regarding ResearchMatch, reach out to the Liaison at IRB@mgsns.org

Recruitment of Students or Employees

The research must not bestow any competitive academic or occupational advantage over other students or staff who do not volunteer. The researchers must not impose any academic or occupational penalty on those not volunteering. One way investigators can reduce the potential to cause undue influence is to design the study so that the instructor, or employer, is blind to the identity of the subjects. If a study is designed in this way, potential subjects should be informed that the Investigator will not know who did and who did not participate. The study should also be designed so that the Investigator cannot infer who participated through indirect means (e.g. by seeing who walks into the laboratory, by getting a list of who earned extra credit for participating in the study, etc.). If extra credit or other rewards are offered for participation in the research study, the Investigator must offer students non-research alternatives for extra credit or other rewards, which involve comparable time and effort to the research.

Due to the potential for undue influence, Investigators should avoid recruiting their employees or students from their own institution/class. Additional protections against undue influence will be required if Investigators must recruit from their own courses. When recruiting students from academic courses where the investigators are not primary course instructors, the Investigators must gain permission from the course professor who is in charge of the course. When recruiting employees or students is the only feasible way to conduct a study, Investigators are expected to design the research in such a way that reduces the potential for subjects to feel pressured (unduly influenced) to participate. In these cases, the informed consent document should clearly state that the decision not to participate or to withdraw participation will not have any consequences (e.g. will not affect course grades, recommendations, access to courses or educational opportunities in the future, consideration for bonus, promotion, work evaluations).

Research Subject Pools

A subject pool is a research resource used by some clinics, departments, and colleges as a registry of individuals who are interested in participating in research and agree to be contacted for potential participation in a study. These volunteers are utilized in studies for that clinic, college, or department. The IRB reviews all research requesting "pool" participation.

Student subject pools serve to not only provide researchers a pool from which to recruit primarily student subjects for their studies, but also serve to familiarize students with the research process as subjects and researchers. Student participation in subject pool research must be completely voluntary. While course credit can be offered for participating, students cannot be penalized or "docked points" for not appearing for a scheduled research appointment. Departments may provide students with incentives to participate in the subject pool; however, reimbursement for participation must not jeopardize subject confidentiality or anonymity. In addition, pools offering extra credit to participating students must provide alternative opportunities to earn the same extra credit for those not wishing to participate in the research. Alternatives to the research subjects should require an equivalent amount of time and effort to complete for extra credit. Subject pools including subjects under eighteen (18) years of age are required to obtain parental permission prior to their involvement in research unless those individuals are emancipated. Subject pool requirements and procedures vary by department so it is best to consult with your individual departments for specific guidelines and additional requirements.

Recruitment of the Research Team and/or Family Members to Participate in Research

The enrollment of spouses, domestic partners, dependents, parents, siblings, grandparents, or research team members presents the perception, whether real or not, of research bias and coercion and is not allowed by the IRB. These individuals can participate in research conducted by the Institution but not in a study in which they are on the study team or an immediate family member of a study team member. The IRB may consider exceptions to this policy in certain extenuating circumstances. Contact the IRB Office at IRB@mgsns.org before enrolling one of these individuals.

If the research is subject to Good Clinical Practice (GCP) requirements, individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention.

Recruitment of Subjects Currently Enrolled in Another Research Study (Dual Enrollment)

Investigators may wish to recruit/enroll subjects who are currently enrolled in another research study. This is referred to as "dual enrollment," and is approvable under certain circumstances. In

order to request dual enrollment with another study, the Investigator must upload a letter or email in Section 3 of the Local Site Documents page of the IRB application from the other study's Investigator agreeing to the dual enrollment. This letter should include the name of the study, the protocol/study number, justification as to why subjects should be enrolled in both studies, and any risks that may occur due to the dual enrollment (e.g. if both studies involve a drug, what those risks could be and how they will be mitigated).

32. How do I document consent?

Use the consent approved by the IRB which has the approval date stamp in the header and watermark in the footer. All items in the signature block, including dates should be completed by the intended party.

The following are the requirements for consent documents:

- The subject or legally authorized representative (LAR) prints their name, signs and dates the consent document themselves.
    - If the subject/representative is physically unable to sign the consent form, note this on the consent form and document the method used for communication with the prospective subject/representative and the specific means by which their agreement was communicated
- LAR is sometimes known as a proxy. In accordance with Florida Statute 765.401(1), healthcare decisions may be made for the patient by certain individuals in order of priority. LAR cannot be utilized unless it is an IRB approved process.
- The individual study staff obtaining consent signs and dates the consent document after the subject signs.
- Whenever the IRB or the sponsor require a witness to the oral presentation, such as when the subject/representative cannot read (visually impaired or illiterate), the witness signs and dates the consent document. The impartial witness to be present during the entire consent discussion to attest that the information in the consent form and any other information provided was accurately explained to, and apparently understood by, the subject/representative, and that consent was freely given. The witness may be a family member or friend. The witness may not be a person involved in the design, conduct, or reporting of the research study. This process should be outlined in the protocol and IRB approved in advance.
- Written assent should be conducted in a similar manner as above. Verbal assent must be documented and that documentation should be saved in the study records.
- A copy of the signed and dated consent document is to be provided to the subject unless otherwise instructed by the IRB, e.g. when retaining a copy would be potentially harmful if seen by others.
- The written and oral consent should contain minimal elements which are outlined in the consent templates. Clinical trial elements are also outlined in Appendix A-3.
- Clinical trials should document additional details supporting that each subject’s informed consent was obtained following International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines, e.g. subject had sufficient time to consider

participation, all questions answered, written consent was obtained prior to any study procedures, etc. Reference Appendix A-3 when unsure. In addition to consent documentation, there should be details documented when a subject withdraws from research, as referenced in Appendix A-1.

- When the IRB approves a digital consent process and/or a digital signature, the principles outlined above are still to be followed unless detailed in the IRB-approved protocol. If the study is FDA or GCP regulated or involves PHI the eConsent platform must be HIPAA and 21 CFR Part 11 compliant, and are approved on a case-by-case basis.

Reference policies HRP-090 - SOP - Informed Consent Process and HRP-091 - SOP: Written Documentation of Consent for more detailed information.

Electronic Signatures on consent documents

Collection of electronic participant signature on a consent document is permissible under certain conditions. The IRB approved stamped consent document must be used unless the protocol indicated otherwise and the IRB approved the process. Investigators are responsible for ensuring that the informed consent form is signed and personally dated by the subject or by the subject's legally acceptable representative (if IRB approved), and by the person who conducted the informed consent discussion prior to a subject's participation in the study. The software platform must be spelled out in detail in the protocol or IRB application and be appropriate for the type of research. E.g., FDA regulated trials requires a system that follows Good Clinical Practice (GCP) Guidelines, Health Insurance Portability and Accountability Act of 1996 (HIPAA) requirements, and FDA's 21 CFR 11 Compliance. At all times, the informed consent forms must be readily accessible for review and/or inspection by applicable regulatory agencies. Departments/colleges should have a more detailed policy in place to ensure responsible oversight, including how the subject's identity will be verified before collection signatures. Any individual consenting subjects should be on the MGS IRB application (whether MGS is the relying or reviewing IRB), trained on the protocol and trained on the software platform to minimize inappropriate processes or errors. Examples of acceptable eConsent platforms are Florence eConsent for FDA Part 11 regulated research, Box.com, RedCap for research requiring HIPAA compliance or DocuSign for non-FDA or HIPAA regulated research. Send questions to IRB or QA-QI@MGS.edu. See Question #29 regarding relying on an external IRB. The external applications when relying on an outside IRB are required to include the consent process inclusive of electronic platforms, as applicable.

33. How do I submit a modification and when is reconsent required?

The Investigator has the responsibility to ensure individuals participating in human subjects research are informed about new information that might affect the subject's willingness to participate in the research study. Changes to the risks or benefits listed in the informed consent document should be submitted to the IRB as a modification and approved by the MGS IRB prior to reconsenting subjects. Subjects should be informed of the changes, asked if they wish to continue to participate, and signify their willingness by signing the amended consent document. Changes can also be documented in an addendum to the informed consent document should the study team choose to not amend the previous consent (this procedure may only be used if subject

recruitment has ended). Minor administrative changes to the informed consent document do not require the reconsenting of subjects who are already participating. Investigators who have questions regarding whether or not subjects should reconsent should contact the MGS IRB.

Complete the modification Form in MGS IRB and attach all requested supplements, then have the Form submitted by the Investigator or PI Proxy by clicking the "Submit" activity. Maintain electronic copies of all information submitted to the IRB in case revisions are required. Please note that research must continue to be conducted without inclusion of the modification until IRB approval is received.

34. What happens if I deviate from my protocol, HRPP policy, or federal regulations?

A protocol deviation is defined as any departure from an IRB approved protocol. Reporting of protocol deviations to the MGS IRB is required regardless of the funding source, study sponsor, or whether the protocol involves an investigational or marketed drug, device, or biological product. All members of the research team are responsible for appropriately reporting deviations from the study protocol to the IRB and any other applicable parties. The Investigator is ultimately responsible for ensuring the prompt reporting of protocol deviations that impact the rights, safety, and welfare of subjects and/or the integrity of the data. The Investigator is responsible for reviewing all protocol deviations to determine if they present a change in the risks and/or benefits to study subjects, and whether any changes in the informed consent document(s), the protocol, or other study-related documents are required. Failure to report protocol deviations in accordance with this policy may be considered serious and/or continuing non-compliance. When MGS is relying on external IRB, obligations vary slightly, refer to Question #30 of this Investigator Manual for more information.

Non-serious protocol deviations should be recorded on an ongoing comprehensive protocol deviation log and submitted to the IRB at the time of continuing review or study closure if a continuing review is not required. Deviation logs will be reviewed by the fully convened IRB or by the IRB Chair or Vice Chair through expedited procedures as a part of the continuing review process. If an Investigator has a high volume of minor deviations and unsure if it rises to the definition of serious, the deviation log can be uploaded into a Reportable New Information (RNI) activity in MGS IRB.

Examples of **non-serious** non-compliance, which can be reported during a continuing review application, can include:

- Omitting or deviating from an IRB-approved protocol procedure in which no safety issues are involved (e.g. conducting study procedure or procedure slightly outside of the expected window).
- Lapse in IRB approval
- Use of an unstamped but otherwise approved consent document

Serious protocol deviations/serious non-compliance are to be submitted to the IRB within five (5) business days of the study team's knowledge of the event. Serious deviations/serious non-compliance should be submitted via a RNI Form in MGS IRB. Reports should include a detailed description of the event and outcome, as well as a description of any changes to the protocol or other corrective actions taken to prevent recurrence. Failure to submit serious deviations/serious non-compliance within five (5) business days constitutes non-compliance with this policy. The IRB may ask for a detailed Corrective and Preventative Action (CAPA) plan. A QA/QI CAPA guidance document is located in the MGS IRB home page. To reiterate, the Investigator is ultimately responsible for ensuring the prompt reporting of protocol deviations that impact the rights, safety, and welfare of subjects and/or the integrity of the data.

Researchers and their staff are expected to self-report all incidents of non-compliance with policy/regulation and protocol deviations regardless of whether the incident is minor and/or sporadic. The IRB will determine whether protocol deviations constitute non-compliance, which can be deemed by the IRB as serious or non-serious, continuing or non-continuing as noted in the IRB approval letter. For allegations of intentional non-compliance or other misconduct, see Question #43 of this Investigator Manual.

Examples of **serious** non-compliance can include, but are not limited to, the following (see Question #27 for additional guidance):

- Performing human subjects research without first obtaining IRB approval or an IRB declaration of exemption.
- Omitting, deviating from or violating the safety provisions of an IRB-approved protocol and/or procedures.
- Violation of institutional policies, state and local laws, federal laws, regulations and any conditions placed on the conduct of the research activity by the MGS IRB.
- Permitting a protocol's IRB approval to expire without stopping all research-related activities and/or submitting a Study Closure application to the IRB.
- Failure to obtain and document informed consent of research subjects unless the appropriate waiver has been approved.

Investigators and their study teams are expected to comply with all ethical standards, institutional policies, state and local laws, federal laws, regulations, and any conditions placed on the conduct of the research by the IRB. All reports or allegations of non-compliance will be investigated and addressed by the MGS Human Research Protection Program (HRPP), the IRB Chairperson(s), the Institutional Official (IO), or the IO's designee.

In order to comply with 45 CFR 46.103(b)(5)(i), 21 CFR 56.108(b)(2) and 38 CFR 16.113 (as applicable), the MGS HRPP will promptly report to the Office for Human Research Protection (OHRP), the US Food and Drug Administration (FDA) and the Veterans Affairs (VA) the necessary information that describes the serious and/or continuing non-compliance affecting human subjects research.

35. How do I submit continuing review?

Within the study's initial IRB approval letter, the IRB will indicate if a continuing review is needed. If the IRB has determined that an expedited study does not require submission of an annual continuing review, the Investigator will be asked to use the "Confirm Ongoing Research" activity in MGS IRB on an annual basis. This activity will be made available within thirty (30) days of the study's anniversary date. If a continuing review is required, complete the Continuing Review Form in MGS IRB within forty-five (45) days of study expiration. Attach a brief summary of research progress in section seven (7) of the Form in addition to any other applicable supplemental documents. The summary should include a brief description of the research activities that have occurred since the last IRB review. This should include items that are not addressed in sections 6 or 7 of the Continuing Review/Study Closure Form. If there have been any protocol deviations or local serious adverse events (SAEs) since the last IRB review, upload a cumulative deviation and/or SAE log in section seven (7) of the Form. Complete the submission of the Form by clicking the "Submit" activity. Maintain electronic copies of all information submitted to the IRB in case revisions are required. Before submitting the research for continuing review, you must determine whether any member of the research staff has a *new* financial interest related to the research. A "yes" or "no" answer is sufficient. See Question #5 of this Investigator Manual for additional information.

As a courtesy, the MGS IRB sends reminders of continuing review to study teams 60, 45, and 30 days prior to study expiration date. However, it is ultimately the Investigator's responsibility to complete and submit an IRB application for continuing review or study closure prior to the annual renewal date.

If the continuing review involves minor modifications to previously approved research, submit those modifications as a combined Modification/Continuing Review application.

If the Investigator does not submit a continuing review or request study closure when required to do so, or if approval has not been granted prior to the expiration of the current IRB approval, the approval will expire. All research activities including enrollment of new subjects and continuation of research interventions or interactions with currently enrolled subjects, ***must stop immediately*** and the HRPP staff will notify the MGS QA/QI Program. If a continuing review is not submitted within thirty (30) calendar days after expiration, a study closure request must be submitted. In order to continue the research, a new submission within MGS IRB is required. Refer to Question #36 of this Investigator Manual for information on closing a study.

If a continuing review is approved pending recertification of a study team member's human subjects protections (HSP) education, the recertification must be provided to the IRB within fifteen (15) business days of the previous study expiration date or the study will lapse in approval. If the study lapses in approval, a new IRB application must be submitted to continue the research.

If IRB approval of human subjects research expires, all human subjects research procedures related to the protocol under review must cease, including recruitment, advertisement, screening,

enrollment, consent, interventions, interactions, and collection or analysis of private identifiable information. Continuing human subjects research procedures is a violation of IRB policy. If current subjects will be harmed by stopping human subjects research procedures that are available outside of the human subjects research context, provide these on a clinical basis, as needed, to protect current subjects. If current subjects will be harmed by stopping human subjects research procedures that are not available outside of the human subjects research context, immediately contact the IRB Chair and provide a de-identified list of the currently enrolled subjects and why they will be harmed by stopping human subjects research procedures.

36. How do I close out a study?

Complete the Continuing Review (CR) Form in MGS IRB. Attach a brief summary of research progress in section seven (7) of the Form in addition to any other applicable supplemental documents. As soon as the research is complete submit the Form by clicking the "Submit" activity. You will indicate that the research has concluded in the submission by selecting the first four specific research milestones within the CR Form Question #4. A study can be closed when all of the following condition are met, unless not applicable:

- Study is permanently closed to enrollment OR was never open for enrollment;
- All subjects have completed all study-related interventions OR not applicable (e.g. study did not include interventions, no subjects were enrolled);
- Collection of private identifiable information is complete OR not applicable (no subjects were enrolled); and
- Analysis of private identifiable information is complete OR not applicable (no subjects were enrolled).

Maintain electronic copies of all information submitted to the IRB in case revisions are required. To avoid study lapse and non-compliance, submit a study closure request within forty-five (45) days before study expiration.

37. How long do I keep records?

Maintain your human subjects paper and digital research records, including the original signed and dated consent documents, for at least five (5) years after completion of the research. If your research is non-FDA, GCP, or HIPAA regulated, there is the ability to approve the digitization of signed and dated HIPAA authorizations and consent documents that include HIPAA authorizations for at least six (6) years after completion of the research. If your research is non-FDA, GCP or HIPAA regulated there is an ability to approve the digitization of research records including signed consents, contact the IRB@mgsns.org to discuss options for your research.

Research data generated as part of MGS research is owned by this Institution or as indicated by a contract. Original source documents, including original data collection assessment tools, signed consent documents and identifiable data, must remain at this Institution for the duration of the applicable record retention period. A researcher may leave this Institution with de-identified

data/documents unless agreements state otherwise, but never original documents. Ensure that the appropriate department personnel have been notified and acknowledge the original source documents that will be staying within the department prior to the researcher's departure.

If your human subjects research is sponsored, contact the sponsor before disposing of human subjects research records. See also Appendix A-2 item 2(d)(iii) for FDA-regulated record retention requirements and Appendix A-3 item 8(e) for Clinical Trials following GCP requirements.

Refer to the "Retention and Destruction of Research Records" guidance document for located in the Regulation and Guidance section of the MGS IRB homepage to ensure you are following current MGS IRB research data storage requirements.

38. What are my obligations to keep records and data private?

All human subjects research reviewed by the MGS IRB, or a MGS-relied upon IRB, must have adequate provisions to protect the privacy of subjects and the confidentiality of data in accordance with the applicable federal regulations, state and local laws, and this Institution's policies and procedures as they relate to research.

Investigators are responsible for ensuring the research is conducted in a manner consistent with the ethical principles outlined in the Belmont Report, the federal regulations, state and local laws, and MGS HRPP policies and procedures. Investigators are responsible for outlining in the protocol the information to be collected as part of the research and the measures that will be taken to protect the confidentiality of the data while the research is being conducted as well as when it is complete.

Investigators must store original hard copy data and documents (including original signed consent documents) and electronic data in a secure location as described in the IRB-approved protocol. The MGS IRB does not allow research data, including informed consents, to be stored in patients' medical records. Research records are propriety, e.g. Sponsor/funders have ownership of the research records as defined within the Clinical Trial Agreement (CTA)/grant, See Appendix A-3 for additional information. Once a subject has been provided with a copy of their signed research consent form, a signed copy of the consent form is retained as part of the research record. It is not permitted to store documents and/or identifiable data at a private residence during conduct of the study nor archiving after it is complete. It is also not acceptable to store identifiable Protected Health Information (PHI) for research purposes on personal computers or portable devices.

Investigators will need to provide access to hard and/or electronic copies of research records, including informed consents, when examiners arrive for inspections. Federal officials have the right to inspect research records, including informed consent documents and individual medical records, to ascertain compliance with the regulations. The FDA requires that information regarding this authority be included in the informed consent document for all research that it regulates. Identifiable information obtained by federal officials during such inspections is subject to both the privacy provisions and the disclosure provisions of the Privacy Act of 1974.

MGS QA/QI program can assist investigators and research teams navigate through an FDA audit by assisting with everything from preparing for the FDA to come on site to being present during the FDA inspection. The office is there to assist in making sure that study systems, processes, and study locations are compliant with federal, state, Institutional and FDA regulations and guidelines. If investigator and/or study teams are already aware of an upcoming FDA inspection, QA/QI Program suggests that they complete the Investigator Self Evaluation form and FDA Tips Checklist as soon as possible.

39. What if I need to use an unapproved drug, biologic, or device for expanded access, compassionate use, or Humanitarian Use?

Unapproved drugs, biologics, and devices can be used for expanded access, compassionate use, or Humanitarian Use with prospective IRB review and approval. To obtain IRB review and approval, a new study submission must be submitted in MGS IRB.

Expanded Access of Drugs and Biologics

Expanded access is the use of investigational new drug products outside of clinical trials for the sole purpose of treating a patient or patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. Types of expanded access include single patient IND, intermediate size patient population, and large patient populations. While expanded access is not considered a clinical investigation, prospective FDA submission and IRB review are required and informed consent must be obtained. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if they are willing to provide the drug or biologic. If the manufacturer agrees to provide the drug, the physician should submit an IND to the appropriate federal review division. The party who submits a request to open an expanded access IND application and receives FDA's authorization to use the investigational product is considered the sponsor of the IND application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, physicians and investigators should recognize that such applications are only suitable when all of the following criteria apply:

- Patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;
- The potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context of the disease or condition to be treated; and
- Providing the investigational drug for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the product.

For non-emergent single patient INDs, an IND application for individual patient use of an investigational drug must be received by the FDA before shipment of and treatment with the

drug may begin. The FDA allows investigators to use FDA's Form 3926 to request, a waiver of the requirement for review and approval of single patient IND applications at a convened IRB meeting. If such waiver is requested and granted by the FDA, expanded access applications for single patient INDs may be reviewed by the IRB Chair via expedited procedures. If an additional patient can benefit from the same treatment, a separate IND application must be submitted to the FDA. Once the FDA acknowledges the IND for the additional patient, the Investigator must submit a modification to the IRB to increase the number of subjects enrolled under the existing application and upload the FDA IND documentation.

Intermediate-size patient population and Treatment INDs (large-patient populations) for expanded access programs must be reviewed at the next available convened IRB meeting. Submit a new application including the program protocol and consent form.

Expanded Access of Medical Devices (a.k.a. Compassionate Use of Devices)

See HRP-325 – WORKSHEET - Device Compassionate Use for additional information. This provision allows access for patients who do not meet the requirements for participation in the clinical investigation but for whom the treating physician believes the device may provide a benefit in treating or diagnosing their disease or condition. The condition must be serious and there must be no available, generally acceptable alternatives for treatment. This provision is typically approved for single patients but may be approved to treat a small group. Prior FDA approval is needed before compassionate use occurs. In order to obtain FDA approval, the sponsor should submit an IDE supplement requesting approval for a protocol deviation. The physician should not treat the patient (or patients) identified in the supplement until FDA and the IRB both approve the use of the device under the proposed circumstances. Compassionate use of devices require prospective IRB review and approval.

Humanitarian Use Devices (HUDs)

See HRP-323 - WORKSHEET - Criteria for Approval HUD for additional information. For a HUD to be used to diagnose or treat an illness/impairment, a Humanitarian Device Exemption (HDE) must be issued by the FDA. The IRB will not grant approval until it has ensured the HDE approval has been granted. The device's labeling must state that the device is a HUD and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been proven or demonstrated.

When a HUD is being used in non-research clinical care, the IRB encourages physicians to obtain prospective and documented informed consent from a patient prior to the use of a HUD, when feasible. This document must not use the term "research" to refer to the activities associated with the use of the device. If informed consent cannot be obtained, information regarding the labeling of the device (i.e. patient information packet), which incorporates information on the device may be used as an alternative. This information must be reviewed in detail with the patient. When the use of a HUD is for diagnosis or treatment, and not associated

with research or data collection, HIPAA regulations for research do not apply as the use of the HUD is part of Treatment, Payment or Operations (TPO).

When an investigator seeks to collect safety and effectiveness data about the device, if the use is within the approved labeling, no IDE is needed; however, IRB approval is required and informed consent must be obtained since the use constitutes research. FDA considers the research to be exempt from the requirement for an IDE as long as the HUD is used in accordance with its approved indication(s). If the Investigator plans to collect data for a new use of the device (a different indication), then the IDE regulations must be followed. If the device is a significant risk device, an FDA approved IDE is required (21 CFR 812.1, 812.20). HUDs being utilized in clinical investigations require prospective IRB approval and informed consent including HIPAA authorization must be obtained.

Whenever an Investigator receives or otherwise becomes aware of information from any source that reasonably suggests an HUD has or may have caused or contributed to the death or serious injury of a patient, or has malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur, the Investigator must report such findings to the FDA and the IRB promptly. Serious injury means an injury or illness that (1) is life-threatening, (2) results in permanent impairment of a body function or permanent damage to a body structure, or (3) necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure (21 CFR 803.3). This reporting is in addition to, not a substitute for, FDA and/or manufacturer reporting requirements in accordance with 21 CFR 803.30. Additionally, the Investigator must promptly report any FDA action(s) regarding the HUD to the MGS IRB.

To submit a request to use an unapproved drug, biologic, or device for expanded access, compassionate use, or Humanitarian Use Device, the PI needs to complete the New Study Form in the MGS IRB system and attach all requested supplements, have the Form submitted by the PI by clicking the “Submit” activity. Maintain electronic copies of all information submitted to the IRB in case revisions are required. Before submitting the application for initial review, you must:

- Obtain the financial interest status (“yes” or “no”) of each individual involved in the clinical care of the patient receiving the HUD.
- Obtain the agreement of each individual involved in the clinical care of the patient receiving the HUD to his/her role.

40. What if I need to use an unapproved drug, biologic, or device and there is no time for IRB review?

See HRP-322 - WORKSHEET - Emergency Use for the regulatory criteria allowing such a use and make sure these are followed. Complete HRP-200 - FORM - Emergency Use of a Test Article and use HRP-506 - Emergency Use or Compassionate Use Consent to prepare your consent document. The IRB requires notification prior to the emergency use of a drug, biologic, or device unless the determination is made after business hours. You will need to submit a report of the use to the IRB within five (5) business days after the use by sending the completed HRP-

200 - FORM - Emergency Use of a Test Article to IRB@mgsns.org. The report should also include a copy of the Investigator's Brochure or device manual if available, and either the consent template that was used or a redacted copy of the signed informed consent form. Under very limited circumstances, the requirements for informed consent may be waived in an emergency situation. For addition-al information regarding notification to the IRB of emergency use of test articles, please contact 800-643-7307 ext. 711. If you fail to submit the report within five (5) business days, you will be in non-compliance.

Emergency use of an unapproved drug or biologic differs from emergency use of an unapproved device in whether it is classified as research or not. Emergency use of an unapproved drug or biologic in a life-threatening situation without prior IRB review is "research" as defined by FDA, the individual getting the test article is a "subject" as defined by FDA, and therefore is governed by FDA regulations for IRB review and informed consent. Emergency use of an unapproved device without prior IRB review is not "research" as defined by FDA and the individual getting the test article is not a "subject" as defined by FDA. However, FDA guidance recommends following similar rules as for emergency use of an unapproved drug or biologic.

Note: The IRB does not allow ***planned*** emergency research.

41. What if I want a non-affiliated individual to assist on MGS research?

There are two different avenues that the MGS IRB allows for non-MGS individuals to work on MGS IRB research projects. The first is using the **MGS Volunteer Appointment** process, which should be used when the individual is performing hours of service for the Graduate School for civic, charitable, or humanitarian reasons, without promise, expectation, or receipt of compensation or future employment for the services rendered. This means that they are not paid and are not performing the same types of duties that someone employed by MGS is performing. These individuals need to be approved by the department of the Investigator and will be required to submit to a Level 1 (or Level 2 depending on the research) background check at the expense of the department. The HR's Volunteer Guidelines contain important information for departments and volunteers. Please take the time to carefully review the guidelines as these have been updated to provide specific information such as: definition of a volunteer, restrictions on use of volunteers, applicability of State Law, responsibilities of the department and volunteer, volunteer benefits, termination of volunteer services, -and record keeping requirements.

Departments hosting volunteer opportunities are required to have the selected volunteer complete both a Volunteer Service Application form and a Volunteer Appointment form. These completed forms must be returned to the Division of Human Resources for review and approval prior to the start of the volunteer services. Volunteer appointments are approved for a maximum of 12 months within the graduate school's academic year. A Volunteer Extension form will be required if extending a volunteer appointment beyond the time period originally approved. Completed forms can be submitted electronically via email at IRB@mgsns.org

In order to be added to an existing MGS IRB project, these individuals will need to have completed the appropriate human subjects training as well as have an ARC account. The CV must indicate that the individual has an approved MGS Volunteer appointment.

Investigator of a study who oversee a volunteer are responsible for the following:

- Making sure the appropriate HR Volunteer forms are submitted and approved. This includes submitting modifications to remove individuals whose volunteer appointments have expired from the study team (per MGS HR policies, volunteer appointments expire at the end of each calendar year).
- Ensuring that all volunteers are qualified by training and experience for their research roles, including knowledge of applicable laws, regulations, codes and guidance, relevant professional standards, and MGS HRPP policies regarding the protection of research subjects.
- Ensuring that all volunteers complete any MGS-required training prior to engaging in the research (e.g. if the volunteer will have access to PHI, ensuring that the volunteer completes HIPAA training).
- Submitting modifications to and obtaining approval from the IRB to add volunteers to a study team, before the volunteers engage in conducting human subjects research.

Individuals requesting a volunteer appointment are responsible for the following:

- Submitting a request for a MGS IRB account, once the background check has been completed and the appointment has been approved by HR. The signed Volunteer Appointment Form and documentation of background check completion will be required before an ARC account will be set up.
- Indicating on the volunteer's CV or resume, which is required in order to obtain a MGS IRB account, the length of the proposed volunteer appointment and the level of the background check that was completed.
- Submitting approved volunteer re-appointment paperwork to the IRB via IRB@mgsns.org, when a previous volunteer appointment expires.

The second way is by using an **Individual Investigator Agreement (IIA)**, which is a written agreement between the MGS IRB and the independent Investigator who is collaborating on MGS research, where MGS is agreeing to extend its oversight to the individual, and by which the independent Investigator agrees to fulfill specified expectations and responsibilities. Currently the MGS IRB is only agreeing to IIAs for federally funded research. There are two separate types of independent investigators:

1) Collaborating **Independent Investigator** who, is not otherwise an employee or agent of the assured Institution (MGS); conducting collaborative research activities outside the facilities of the assured Institution (MGS); and not acting as an employee of any

institution with respect to his or her involvement in the research being conducted by the assured institution.

2) Collaborating **Institutional Investigator** who, is not otherwise an employee or agent of the assured Institution (MGS); conducting collaborative research activities outside the facilities of the assured Institution (MGS); acting as an employee or agent of a non-assured institution with respect to his or her involvement in the research being conducted by the assured Institution (MGS); and employed by, or acting as an agent of, a non-assured institution that does not routinely conduct human subjects research.

These individuals will still need to have the appropriate human subjects training. If an individual meets the definition of either of the two types of independent investigators above, contact the IRB at IRB@mgsns.org to determine the training and documentation that will be required.

42. How do I get additional information and answers to questions?

This document and the policies and procedures for the MGS Human Research Protection Program are available on the IRB website at https://masgutovagraduateschool.com/student-services/institutional-review-board-irb

If you have any questions or concerns, about the Human Research Protection Program, contact the IRB Office at:

MGS Institutional Review Board
6718 Lake Nona Blvd., Suite 180
Orlando, FL 32827
IRB@mgsns.org
Phone: 800-643-7307

If you have questions, concerns, complaints, allegations of undue influence, allegations or findings of non-compliance, or input regarding the Human Research Protection Program that cannot be addressed by contacting the IRB Office, follow the directions in the HRP-101 - HUMAN RESEARCH PROTECTION PROGRAM PLAN under "Reporting and Management of Concerns."

43. How can I make an anonymous report about suspected research misconduct?

Concerns, complaints, or allegations regarding the conduct of human subjects' research, the actions, policies, or procedures of the IRB members, IRB administrators, or IRB staff must be appropriately investigated and handled in a consistent and timely manner.

IRB members, staff, faculty, study teams, students, research subjects, or any other person who has a concern or complaint or feels they have been subjected to or witnessed coercion or undue influence can contact Research Integrity and Compliance (RIC) at:

MGS Institutional Review Board
6718 Lake Nona Blvd., Suite 180
Orlando, FL 32827

IRB@mgsns.org
Phone: 800-643-7307

These concerns/complaints are accepted in any format including verbal, written, or electronic. Reports of concerns, complaints, or allegations of coercion, undue influence, research misconduct or non-compliance are thoroughly investigated. If necessary, corrective action is taken to correct the situation and/or protect subjects in research. The Organizational Official (OO) or designee is ultimately responsible for ensuring that all concerns, complaints, and allegations have been addressed appropriately.

The person being notified of the concern/complaint forwards it to the highest level administrator within the HRPP or the Office of Research & Innovation as is necessary to receive appropriate attention and actions. Allegations that include issues that appear to constitute research misconduct will be reported to the Research Integrity Officer (RIO) and handled pursuant to the process outlined in MGS Policy 0-301. There may be situations in which both HRPP policies and MGS Policy 0-301 apply. In such cases, both policies will be followed.

The Masgutova Graduate School of Neurodevelopmental Sciences

Appendices[1]

Appendix A-1 Additional Requirements for DHHS-Regulated Research[2]

1. When a subject decides to withdraw from a clinical trial, the Investigator conducting the clinical trial should ask the subject to clarify whether the subject wishes to withdraw from all components of the trial or only from the primary interventional component of the trial. If the latter, research activities involving other components of the clinical trial, such as follow-up data collection activities, for which the subject previously gave consent may continue. The Investigator should explain to the subject who wishes to withdraw the importance of obtaining follow-up safety data about the subject.
2. Investigators are allowed to retain and analyze already collected data relating to any subject who chooses to withdraw from a research study or whose participation is terminated by an investigator without regard to the subject's consent, provided such analysis falls within the scope of the analysis described in the IRB-approved protocol. This is the case even if that data includes identifiable private information about the subject.
3. For research not subject to regulation and review by FDA, investigators, in consultation with the funding agency, can choose to honor a research subject's request that the Investigator destroy the subject's data or that the Investigator exclude the subject's data from any analysis.
4. When seeking the informed consent of subjects, investigators should explain whether already collected data about the subjects will be retained and analyzed even if the subjects choose to withdraw from the research.
5. For federally-funded research involving genomic testing, see HRP-064 – SOP - NIH GDS Institutional Certification and HRP-332 – WORKSHEET - NIH GDS Institutional Certification for additional requirements and guidance, including information about dbGaP and GWAS.

[1] The following appendices contain additional regulatory requirements. When MGS HRPP policies and the applicable federal regulatory requirements differ, the stricter policy/requirement applies.
[2] http://www.hhs.gov/ohrp/policy/subjectwithdrawal.html

Appendix A-2 Additional Requirements for FDA-Regulated Research

1. Investigators are responsible for determining whether research in which they are engaged requires an IND or IDE and, if so, for securing the necessary approvals.
2. The regulations may permit a sponsor to charge for an investigational drug, biologic, or device.
3. Investigator-sponsors must comply with all applicable FDA regulations. For additional information, see HRP-306 - WORKSHEET - Drugs and Biologics and HRP-307 - WORKSHEET – Devices.
4. See Appendix A-3 item for clinical trial registration and results reporting (clinicaltrials.gov).
5. For FDA-regulated research involving investigational drugs:
    a. Investigators must abide by FDA restrictions on promotion of investigational drugs:[3]
        i. An investigator, or any person acting on behalf of an investigator, must not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug.
        ii. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.
        iii. An investigator must not commercially distribute or test market an investigational new drug.
    b. Follow FDA requirements for general responsibilities of investigators[4]
        i. An investigator is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation.
        ii. An investigator must, in accordance with the provisions of 21 CFR §50, obtain the informed consent of each human subject to whom the drug is administered, except as provided in 21 CFR §50.23 or §50.24 of this chapter.
        iii. Additional specific responsibilities of clinical investigators are set forth in this part and in 21 CFR §50 and 21 CFR §56.
    c. Follow FDA requirements for control of the investigational drug[5]

[3] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.7
[4] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.60
[5] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.61

i. An investigator must administer the drug only to subjects under the Investigator's personal supervision or under the supervision of a sub-investigator responsible to the Investigator.
ii. The Investigator must not supply the investigational drug to any person not authorized under this part to receive it.

d. Follow FDA requirements for investigator recordkeeping and record retention[6]
   i. Disposition of drug:
      1. An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects.
      2. If the investigation is terminated, suspended, discontinued, or completed, the Investigator must return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR §312.59.
   ii. Case histories.
      1. An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation.
      2. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. The case history for each individual must document that informed consent was obtained prior to participation in the study.
   iii. Record retention: An investigator must retain required records for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.

e. Follow FDA requirements for investigator reports[7]
   i. Progress reports: The Investigator must furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.
   ii. Safety reports: An investigator must promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the Investigator must report the adverse effect immediately.
   iii. Final report: An investigator must provide the sponsor with an adequate report shortly after completion of the Investigator's participation in the investigation.

[6] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.62
[7] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.64

iv. Financial disclosure reports:
    1. The clinical investigator must provide the sponsor with sufficient accurate financial information to allow an applicant to submit complete and accurate certification or disclosure statements as required under 21 CFR §54.
    2. The clinical investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study.

f. Follow FDA requirements for assurance of IRB review[8]
    i. An investigator must assure that an IRB that complies with the requirements set forth in 21 CFR §56 will be responsible for the initial and continuing review and approval of the proposed clinical study.
    ii. The Investigator must also assure that he or she will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risk to human subjects or others, and that he or she will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

g. Follow FDA requirements for inspection of investigator's records and reports[9]
    i. An investigator must upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the Investigator pursuant to 312.62.
    ii. The Investigator is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.

h. Follow FDA requirements for handling of controlled substances[10]
    i. If the investigational drug is subject to the Controlled Substances Act, the Investigator must take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.

6. For FDA-regulated research involving investigational devices:
    a. General responsibilities of investigators.[11]
        i. An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the Investigator's care, and for the control of devices

[8] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.66
[9] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.68
[10] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.69
[11] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.100

under investigation. An investigator also is responsible for ensuring that informed consent is obtained in accordance with 21 CFR §50.

ii. The significant risk (SR)/non-significant risk (NSR) determination for devices is made initially by the sponsor or investigator-sponsor.

b. Specific responsibilities of investigators[12]
   i. Awaiting approval: An investigator may determine whether potential subjects would be interested in participating in an investigation, but must not request the written informed consent of any subject to participate, and must not allow any subject to participate before obtaining IRB and FDA approval.
   ii. Compliance: An investigator must conduct an investigation in accordance with the signed agreement with the sponsor, the investigational plan, and other applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.
   iii. Supervising device use: An investigator must permit an investigational device to be used only with subjects under the Investigator's supervision. An investigator must not supply an investigational device to any person not authorized to receive it.
   iv. Financial disclosure:
      1. A clinical investigator must disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements required under 21 CFR §54.
      2. The Investigator must promptly update this information if any relevant changes occur during the course of the investigation and for one (1) year following completion of the study.
   v. Disposing of device: Upon completion or termination of a clinical investigation or the Investigator's part of an investigation, or at the sponsor's request, an investigator must return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.

c. Maintain the following accurate, complete, and current records relating to the Investigator's participation in an investigation:[13]
   i. All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.
   ii. Records of receipt, use or disposition of a device that relate to:
      1. The type and quantity of the device, the dates of its receipt, and the batch number or code mark.
      2. The names of all persons who received, used, or disposed of each device.
      3. Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.

[12] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.110
[13] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.140

iii. Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. Such records must include:
    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 justifying the failure to obtain informed consent.
    2. Documentation that informed consent was obtained prior to participation in the study.
    3. All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), 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.

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

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

d. Inspections[14]

i. Entry and inspection: A sponsor or an investigator who has authority to grant access must permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept).

ii. Records inspection: A sponsor, IRB, or investigator, or any other person acting on behalf of such a person with respect to an investigation, must permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.

iii. Records identifying subjects: An investigator must permit authorized FDA employees to inspect and copy records that identify subjects, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the Investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

[14] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.145

e. Prepare and submit the following complete, accurate, and timely reports[15]
   i. Unanticipated adverse device effects. An investigator must submit to the sponsor and to the Reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than ten (10) working days after the Investigator first learns of the effect.
   ii. Withdrawal of IRB approval. An investigator must report to the sponsor, within five (5) working days, a withdrawal of approval by the Reviewing IRB of the Investigator's part of an investigation.
   iii. Progress. An investigator must submit progress reports on the investigation to the sponsor, the monitor, and the Reviewing IRB at regular intervals, but in no event less often than yearly.
   iv. Deviations from the investigational plan:
      1. An investigator must notify the sponsor and the Reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency.
      2. Such notice must be given as soon as possible, but in no event later than five (5) working days after the emergency occurred.
      3. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and IRB also is required.
   v. Informed consent. If an investigator uses a device without obtaining informed consent, the Investigator must report such use to the sponsor and the Reviewing IRB within five (5) working days after the use occurs.
   vi. Final report. An investigator must, within three (3) months after termination or completion of the investigation or the Investigator's part of the investigation, submit a final report to the sponsor and the Reviewing IRB.
   vii. Other. An investigator must, upon request by a Reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

7. When a subject withdraws from a study:[16]
   a. The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed.
   b. An investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart

[15] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.150
[16] http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126489.pdf

review, and address the maintenance of privacy and confidentiality of the subject's information.

c. If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous bullet, the Investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). IRB approval of informed consent documents is required.
d. If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the Investigator must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent.
e. An investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.

FDA Guidance on E6(R2) GCP: https://www.fda.gov/media/93884/download

Appendix A-3 Additional Requirements for Clinical Trials (ICH-GCP)

1) Investigator's Qualifications and Agreements
    a. The clinical trial should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practice and the applicable regulatory requirements.
    b. The Investigator should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirements, and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB, and/or the regulatory authorities.
    c. The Investigator should be thoroughly familiar with the appropriate use of the investigational product, as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.
    d. The Investigator should be aware of, and should comply with, GCP and the applicable regulatory requirements.
    e. The Investigator/institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authorities.
    f. The Investigator should maintain a list of appropriately qualified persons to whom the Investigator has delegated significant trial-related duties.
2) Adequate Resources
    a. The Investigator should be able to demonstrate (e.g. based on retrospective data) a potential for recruiting the required number of suitable subjects within the agreed recruitment period.
    b. The Investigator should have sufficient time to properly conduct and complete the trial within the agreed trial period.
    c. The Investigator should have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.
    d. The Investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product, and their trial-related duties and functions.
3) Medical Care of Trial Subjects
    a. A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions.
    b. During and following a subject's participation in a trial, the Investigator/institution should ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the trial. The Investigator/institution should inform a subject when medical care is needed for intercurrent illnesses of which the Investigator becomes aware.

c. It is recommended that the Investigator inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.
d. Although a subject is not obliged to give his/her reasons for withdrawing prematurely from a trial, the Investigator should make a reasonable effort to ascertain the reasons, while fully respecting the subject's rights.

4) Communication with IRB
   a. Before initiating a trial, the Investigator/institution should have written and dated approval notification from the IRB for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g. advertisements), and any other written information to be provided to subjects.
   b. As part of the Investigator's/institution's written application to the IRB, the Investigator/institution should provide the IRB with a current copy of the Investigator's Brochure. If the Investigator's Brochure is updated during the trial, the Investigator/institution should supply a copy of the updated Investigator's Brochure to the IRB.
   c. During the trial the Investigator/institution should provide to the IRB all documents subject to review.
5) Compliance with Protocol
   a. The Investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authorities and which was given approval notification by the IRB. The Investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.
   b. The Investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval from the IRB via a modification application, except where necessary to eliminate an immediate hazards to trial subjects, or when the changes involves only logistical or administrative aspects of the trial (e.g. change in monitors, change of telephone numbers).
   c. The Investigator, or person designated by the Investigator, should document and explain any deviation from the approved protocol.
   d. The Investigator may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard to trial subjects without prior IRB approval notification. As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol modifications should be submitted: a) to the IRB for review and approval, b) to the sponsor for agreement and, if required, c) to the regulatory authorities.
6) Investigational Product
   a. Responsibility for investigational product accountability at the trial site rests with the Investigator/institution.
   b. Where allowed/required, the Investigator/institution may/should assign some or all of the Investigator's/institution's duties for investigational product

accountability at the trial site to an appropriate pharmacist or another appropriate individual who is under the supervision of the Investigator/institution.

c. The Investigator/institution and/or a pharmacist or other appropriate individual, who is designated by the Investigator/institution, should maintain records of the product's delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused product. These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product and trial subjects. Investigators should maintain records that document adequately that the subjects were provided the doses specified by the protocol and reconcile all investigational product received from the sponsor.
d. The investigational product should be stored as specified by the sponsor and in accordance with applicable regulatory requirements.
e. The Investigator should ensure that the investigational product is used only in accordance with the approved protocol.
f. The Investigator, or a person designated by the Investigator/institution, should explain the correct use of the investigational product to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.
g. Randomization Procedures and Unblinding: The Investigator should follow the trial's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the trial is blinded, the Investigator should promptly document and explain to the sponsor any premature unblinding (e.g. accidental unblinding, unblinding due to a serious adverse event) of the investigational product.

7) Informed Consent of Trial Subjects
   a. In obtaining and documenting informed consent, the Investigator should comply with the applicable regulatory requirements, and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the trial, the Investigator should have the IRB's written approval notification of the written informed consent form and any other written information to be provided to subjects.
   b. The written informed consent form and any other written information to be provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject’s consent. Any revised written informed consent form, and written information should receive the IRB's approval in advance of use. The subject or the subject’s legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject’s willingness to continue participation in the trial. The communication of this information should be documented.
   c. Neither the Investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial.

d. None of the oral and written information concerning the trial, including the written informed consent form, should contain any language that causes the subject or the subject's legally acceptable representative to waive or to appear to waive any legal rights, or that releases or appears to release the Investigator, the institution, the sponsor, or their agents from liability for negligence.
e. The Investigator, or a person designated by the Investigator, should fully inform the subject or, if the subject is unable to provide informed consent, the subject's legally acceptable representative, of all pertinent aspects of the trial including the written information and the approval opinion by the IRB.
f. The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the subject or the subject's legally acceptable representative and the impartial witness, where applicable.
g. Before informed consent may be obtained, the Investigator, or a person designated by the Investigator, should provide the subject or the subject's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the subject or the subject's legally acceptable representative.
h. Prior to a subject's participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion. The person who conducted the informed consent discussion should sign and date the consent after the subject or by the subject's legally acceptable representative signs/dates the consent.
i. If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to subjects, is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject's legally acceptable representative.
j. Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following:
    i. That the trial involves research.
    ii. The purpose of the trial.

iii. The trial treatments and the probability for random assignment to each treatment.
iv. The trial procedures to be followed, including all invasive procedures.
v. The subject's responsibilities.
vi. Those aspects of the trial that are experimental.
vii. The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.
viii. The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
ix. The alternative procedures or courses of treatment that may be available to the subject, and their important potential benefits and risks.
x. The compensation and/or treatment available to the subject in the event of trial related injury.
xi. The anticipated prorated payment, if any, to the subject for participating in the trial.
xii. The anticipated expenses, if any, to the subject for participating in the trial.
xiii. That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.
xiv. That the monitors, the auditors, the IRB, and the regulatory authorities will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.
xv. That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject’s identity will remain confidential.
xvi. That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.
xvii. The persons to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.
xviii. The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.
xix. The expected duration of the subject's participation in the trial.
xx. The approximate number of subjects involved in the trial.

k. Prior to participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated written informed consent form and any other written information provided to the subjects. During a

subject's participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated consent form updates and a copy of any modifications to the written information provided to subjects.

l. When a clinical trial (therapeutic or non-therapeutic) includes subjects who can only be enrolled in the trial with the consent of the subject's legally acceptable representative (e.g. minors, or patients with severe dementia), the subject should be informed about the trial to the extent compatible with the subject's understanding and, if capable, the subject should sign and personally date the written informed consent.

m. Except as described above, a non-therapeutic trial (i.e. a trial in which there is no anticipated direct clinical benefit to the subject), should be conducted in subjects who personally give consent and who sign and date the written informed consent form.

n. Non-therapeutic trials may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled: a) The objectives of the trial cannot be met by means of a trial in subjects who can give informed consent personally. b) The foreseeable risks to the subjects are low. c) The negative impact on the subject's well-being is minimized and low. d) The trial is not prohibited by law. e) The approval opinion of the IRB is expressly sought on the inclusion of such subjects, and the written approval notification covers this aspect. Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

o. In emergency situations, when prior consent of the subject is not possible, the consent of the subject's legally acceptable representative, if present, should be requested. When prior consent of the subject is not possible, and the subject's legally acceptable representative is not available, enrolment of the subject should require measures described in the protocol and/or elsewhere, with documented approval notification by the IRB, to protect the rights, safety and well-being of the subject and to ensure compliance with applicable regulatory requirements. The subject or the subject's legally acceptable representative should be informed about the trial as soon as possible and consent to continue and other consent as appropriate should be requested.

8) Records and Reports

a. The Investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.

b. Data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.

c. Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained); this applies to both written and electronic changes or corrections. Sponsors should provide guidance to investigators and/or the Investigator's

designated representatives on making such corrections. Sponsors should have written procedures to assure that changes or corrections in CRFs made by sponsor's designated representatives are documented, are necessary, and are endorsed by the Investigator. The Investigator should retain records of the changes and corrections.

d. The Investigator/institution should maintain the trial documents as specified in Essential Documents for the Conduct of a Clinical Trial and as required by the applicable regulatory requirements. The Investigator/institution should take measures to prevent accidental or premature destruction of these documents.
e. Essential documents should be retained until at least two (2) years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least two (2) years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period however if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the Investigator/institution as to when these documents no longer need to be retained.
f. The financial aspects of the trial should be documented in an agreement between the sponsor and the Investigator/institution.
g. Upon request of the monitor, auditor, IRB, or regulatory authority, the Investigator/institution should make available for direct access all requested trial-related records.
h. Investigators of clinical trials are responsible for registering on clinicaltrials.gov as required by federal regulation.

9) Progress Reports
   a. The Investigator should submit written summaries of the trial status to the IRB annually, or more frequently, if requested by the IRB.
   b. The investigator should promptly provide written reports to the sponsor, the IRB and, where applicable, the institution on any changes significantly affecting the conduct of the trial, and/or increasing the risk to subjects.
10) Safety Reporting
   a. All serious adverse events (SAEs) should be reported immediately, within 5 days of knowledge, to the IRB and sponsor except for those SAEs that the protocol or other document (e.g. Investigator's Brochure) identifies as not needing immediate reporting. The immediate reports should be followed promptly by detailed, written reports. The immediate and follow-up reports should identify subjects by unique code numbers assigned to the trial subjects rather than by the subjects' names, personal identification numbers, and/or addresses. The Investigator must comply with the applicable regulatory requirements related to the reporting of unexpected SAEs to the regulatory authorities and the IRB. SAEs that are expected or unrelated are to be submitted during continuing review.
   b. Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor according to the

reporting requirements and within the time periods specified by the sponsor in the protocol.

c. For reported deaths, the Investigator should supply the sponsor and the IRB with any additional requested information (e.g. autopsy reports and terminal medical reports).

11) Premature Termination or Suspension of a Trial
    a. If the trial is prematurely terminated or suspended for any reason, the Investigator/institution should promptly inform the trial subjects, should assure appropriate therapy and follow-up for the subjects, and, where required by the applicable regulatory requirements, should inform the regulatory authorities. In addition:
        i. If the Investigator terminates or suspends a trial without prior agreement of the sponsor, the Investigator should inform the institution where applicable, and the Investigator/institution should promptly inform the sponsor and the IRB and should provide the sponsor and the IRB a detailed written explanation of the termination or suspension.
        ii. If the sponsor terminates or suspends a trial, the Investigator should promptly inform the institution where applicable and the Investigator/institution should promptly inform the IRB and provide the IRB a detailed written explanation of the termination or suspension.
        iii. If the IRB terminates or suspends its approval opinion of a trial, the Investigator should inform the institution where applicable and the Investigator/institution should promptly notify the sponsor and provide the sponsor with a detailed written explanation of the termination or suspension.
12) Final Reports by Investigator: Upon completion of the trial, the Investigator, where applicable, should inform the institution; the Investigator/institution should provide the IRB with a summary of the trial's outcome, and the regulatory authorities with any reports required.

ICH Good Clinical Practice (GCP) Rev 2:
https://www.ich.org/products/guidelines/efficacy/efficacy-single/article/integrated-addendum-good-clinical-practice.html

ICH Efficacy Guidelines to which all researchers should be aware:
https://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html

ClinicalTrials.gov Registration requirements

Appendix A-4 Additional Requirements for Department of Defense (DOD) research

1. When appropriate, research protocols must be reviewed and approved by the IRB prior to the Department of Defense approval. Consult with the Department of Defense funding component to see whether this is a requirement.
2. Civilian researchers attempting to access military volunteers should seek collaboration with a military researcher familiar with service-specific requirements.
3. Employees of the Department of Defense (including temporary, part-time, and intermittent appointments) may not be able to legally accept payments to participate in research and should check with their supervisor before accepting such payments. Employees of the Department of Defense cannot be paid for conducting research while on active duty.
4. Service members must follow their command policies regarding the requirement to obtain command permission to participate in research involving human subjects while on-duty or off-duty.
5. Components of the Department of Defense might have stricter requirements for research-related injury than the DHHS regulations.
6. There may be specific educational requirements or certification required.
7. When assessing whether to support or collaborate with this institution for research involving human subjects, the Department of Defense may evaluate this institution's education and training policies to ensure the personnel are qualified to perform the research.
8. When research involves U.S. military personnel, policies and procedures require limitations on dual compensation:
    a. Prohibit an individual from receiving pay of compensation for research during duty hours.
    b. An individual may be compensated for research if the subject is involved in the research when not on duty.
    c. Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to $50 for each blood draw.
    d. Non-Federal persons may be compensated for research participating other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.
9. Surveys performed on DOD personnel must be submitted, reviewed, and approved by the DOD Information Management Control Officer (IMCO) after the research protocol is reviewed and approved by the IRB. When a survey crosses DOD components, additional review is required. Consult with the Department of Defense funding component to coordinate this review.
10. When research involves large scale genomic data (LSGD) collected on DOD-affiliated personnel, additional protections are required:

a. Additional administrative, technical, and physical safeguards to prevent disclosure of DoD-affiliated personnel's genomic data commensurate with risk (including secondary use or sharing of de-identified data or specimens)
b. Research will apply an HHS Certificate of Confidentiality
c. DoD Component security review

11. Data or information sent to a DOD component under a pledge of confidentiality for exclusively statistical purposes must be used exclusively for statistical purposes and may not be disclosed in identifiable form for any other purpose, except with the informed consent of the respondent.
12. When conducting multi-site research, a formal agreement between institutions is required to specify the roles and responsibilities of each party.
13. The following must be reported to the applicable DOD Component Office of Human Research Protections within 30 days:
    a. When significant changes to the research protocol are approved by the IRB or EC:
        i. Changes to key investigators or institutions.
        ii. Decreased benefit or increased risk to participants in greater than minimal risk research.
        iii. Addition of vulnerable populations as participants.
        iv. Addition of DOD-affiliated personnel as participants.
        v. Change of reviewing IRB.
    b. When the organization is notified by any federal body, state agency, official governing body of a Native American or Alaskan native tribe, other entity, or foreign government that any part of an HRPP is under investigation for cause involving a DOD-supported research protocol.
    c. Any problems involving risks to participants or others, suspension or termination of IRB approval, or any serious or continuing noncompliance pertaining to DOD-supported human participant research.
    d. The results of the IRB's continuing review, if required.
    e. Change in status when a previously enrolled participant becomes pregnant, or when the researcher learns that a previously enrolled participant is pregnant, and the protocol was not reviewed and approved by the IRB in accordance with 45 CFR 46, Subpart B.
    f. Change in status when a previously enrolled participant becomes a prisoner, and the protocol was not reviewed and approved by the IRB in accordance with 32 CFR 219, Subpart C.
    g. Closure of a DOD-supported study.
14. For human participant research that would not otherwise be approved but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates, written approval from the DOD Office for Human Research Protections must be obtained through the DOD Component Office of Human Research Protections prior to research starting.

15. Other specific requirements of the Department of Defense research be found in the "Additional Requirements for Department of Defense (DOD) Research" section in the IRB's HRP-318 – WORKSHEET - Additional Federal Criteria.

Appendix A-5 Additional Requirements for Department of Energy (DOE) Research

(See DOE Order 443.1C)

1. Research that involves one or more of the following must be submitted to the appropriate IRB for human subjects research review and determination:
    a. Study of humans in a systematically modified environment. These studies include but are not limited to intentional modification of the human environment:
        i. Study of human environments that use tracer chemicals, particles or other materials to characterize airflow.
        ii. Study in occupied homes or offices that:
            1. Manipulate the environment to achieve research aims.
            2. Test new materials.
            3. Involve collecting information on occupants' views of appliances, materials, or devices installed in their homes or their energy-saving behaviors through surveys and focus groups.
    b. Use of social media data.
    c. Human Terrain Mapping (HTM).
    d. All exempt HSR determinations must be made by the appropriate IRB and/or IRB office.
2. Personally identifiable information collected and/or used during HSR projects must be protected in accordance with the requirements of DOE Order 206.1, Department of Energy Privacy Program, current version. The Central DOE IRBs require submission of DOE's HRP- 490-CHECKLIST-Reviewing Protocols that use Personally Identifiable Information (PII) if your research includes PII.
3. You must report the following to the DOE human subjects research Program Manager (and, when an NNSA element is involved, the NNSA HSP Program Manager) prior to initiation of any new human subjects research project, even if it meets the regulatory definition of exempt human subjects research as outlined in 10 CFR Part 745.104, involving:
    a. An institution without an established Institutional Review Board (IRB);
    b. A foreign country;
    c. The potential for significant controversy (e.g., negative press or reaction from stakeholder or oversight groups);
    d. Research subjects in a protected class (prisoners, children, individuals with impaired decision making capability, or DOE/NNSA federal or DOE/NNSA contractor employees as human subjects, who may be more vulnerable to coercion and undue influence to participate) that is outside of the Reviewing IRB's typical range/scope; or
    e. The generation or use of classified information.
4. The IRB must be notified immediately and the DOE HSP Program Manager (and, when an NNSA element is involved, the NNSA HSP Program Manager) must be notified

within 48 hours and consulted regarding planned corrective actions if any of the following occur:

a. Adverse events. Notify the IRB for all adverse events and the DOE/NNSA HSP Program Manager if the IRB determines them to be significant, as defined in DOE Order 443.1C.
b. Unanticipated problems and complaints about the research.
c. Any suspension or termination of IRB approval of research.
d. Any significant non-compliance with HSP Program procedures or other requirements.
e. Any finding of a suspected or confirmed data breach involving PII in printed or electronic form. Report immediately to the IRB, the DOE/NNSA HSP Program Manager(s), and the DOE-Cyber Incident Response Capability, in accordance with the requirements of the CRD associated with DOE O 206.1.
f. Serious adverse events and corrective actions taken must be reported immediately to the IRB and the DOE/NNSA HSP Program Manager(s). The time frame for "immediately" is defined as upon discovery.

5. Requirements for human participant protections for classified research apply to all classified research conducted or supported by the DOE and its national laboratories, including contracts, and including Human Terrain Mapping research.
6. Researchers conducting human subjects research in any other country or on citizens or other individuals residing in that country must be cognizant of country-specific human subjects research requirements and consult the IRB regarding applicability of such requirements.
7. No human subjects research conducted with DOE funding, at DOE entities (regardless of funding source), or by DOE or DOE contractor personnel (regardless of funding source or location conducted), whether done domestically or in an international environment, including classified and proprietary research, may be initiated without both a Federalwide Assurance (FWA) or comparable assurance (e.g., Department of Defense assurance) of compliance and approval by the cognizant Institutional Review Board (IRB) in accordance with 10 CFR §745.103. Human subjects research involving multiple DOE sites (e.g., members of the research team from more than one DOE site and/or data or human subjects from more than one DOE site) must be reviewed and approved by one of the Central DOE IRBs prior to initiation, or if authorized by the DOE and/or NNSA HSP Program Manager, other appropriate IRB of record. In all cases, an IRB Authorization Agreement (IAA) or Memorandum of Understanding (MOU) must be in place between the organization(s) conducting the HSR and the organization responsible for IRB review.
8. Human subjects research that involves DOE Federal and/or contractor employees must first be reviewed and approved by the appropriate DOE IRB (the DOE site IRB or one of the Central DOE IRBs), or if deemed more fitting by the Federally assured DOE site or Headquarters, other appropriate IRB of record, in accordance with an IAA or MOU negotiated between the DOE site or Headquarters and the organization responsible for IRB review.

9. Classified and unclassified human subjects research that is funded through the Strategic Intelligence Partnership Program (SIPP) must be reviewed and approved by the Central DOE IRB-Classified.
10. If applicable, federally funded HSR must comply with the requirements of the Paperwork Reduction Act.
11. Other specific requirements of the DOE research can be found in the "Additional Requirements for Department of Energy (DOE) Research" section in the IRB's HRP-318 – WORKSHEET - Additional Federal Criteria.

Appendix A-6 Additional Requirements for Department of Justice (DOJ) Research

Additional Requirements for DOJ Research conducted in the Federal Bureau of Prisons

1. Implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.
2. The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.
3. The research design must be compatible with both the operation of prison facilities and protection of human subjects.
4. Investigators must observe the rules of that institution or office in which the research is conducted and those of the investigator, whichever is strictest.
5. Any investigator who is a non-employee of the Bureau of Prisoners must sign a statement in which the Investigator agrees to adhere to the requirements of 28 CFR §512.
6. The research must be reviewed and approved by the Bureau Research Review Board.
7. Incentives cannot be offered to help persuade inmate subjects to participate. However, soft drinks and snacks to be consumed at the test setting may be offered. Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research subjects who are both: No longer in Bureau of Prisons custody. Participating in authorized research being conducted by Bureau employees or contractors.
8. A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency.
9. Except as noted in the consent statement to the subject, you must not provide research information that identifies a subject to any person without that subject's prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertain.
10. Except for computerized data records maintained at an official DOJ site, records that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system.

11. If you are conducting a study of special interest to the Office of Research and Evaluation but the study is not a joint project involving Office of Research and Evaluation, you may be asked to provide Office of Research and Evaluation with the computerized research data, not identifiable to individual subjects, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.
12. Required elements of disclosure additionally include:
    a. Identification of the investigators.
    b. Anticipated uses of the results of the research.
    c. A statement that participation is completely voluntary and that the subject may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable).
    d. A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, an investigator may not guarantee confidentiality when the subject indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the subject is an inmate, indicates intent to leave the facility without authorization.
    e. A statement that participation in the research project will have no effect on the inmate subject's release date or parole eligibility.
13. You must have academic preparation or experience in the area of study of the proposed research.
14. The IRB application must include a statement regarding assurances and certification required by federal regulations, if applicable.
15. You must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor.
16. At least once a year, you must provide the Chief, Office of Research and Evaluation, with a report on the progress of the research.
17. At least twelve (12) working days before any report of findings is to be released, you must distribute one copy of the report to each of the following: the chairperson of the Bureau Research Review Board, the regional director, and the warden of each location that provided data or assistance.
18. You must include an abstract in the report of findings.
19. In any publication of results, you must acknowledge the Bureau's participation in the research project.
20. You must expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.
21. Prior to submitting for publication the results of a research project conducted under this subpart, You must provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.
22. Other specific requirements of the DOJ Research Conducted within the Federal Bureau of Prisons (BOP) can be found in the “Additional Requirements for Department of Justice

(DOJ) Research Conducted within the Federal Bureau of Prisons (BOP)" section in the IRB's HRP-318 – WORKSHEET - Additional Federal Criteria.

Additional Requirements for DOJ Research Funded by the National Institute of Justice

1. The project must have a privacy certificate approved by the National Institute of Justice Human Subjects Protection Officer.
2. All investigators and research staff are required to sign employee confidentiality statements, which are maintained by the responsible investigator.
3. The confidentiality statement on the consent document must state that confidentiality can only be broken if the subject reports immediate harm to subjects or others.
4. Under a privacy certificate, investigators and research staff do not have to report child abuse unless the subject signs another consent document to allow child abuse reporting.
5. A copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, or other relevant research materials.
    a. At least once a year, the researcher shall provide the Chief, Office of Research and Evaluation, with a report of the progress of the research.
    b. At least 12 working days before any report of findings is to be released, the researcher shall distribute one copy of the report to each of the following: the chairperson of the Bureau Research Review Board, the regional director, and the warden of each location that provided data or assistance. The researcher shall include an abstract in the report of findings.
    c. In any publication of results, the researcher shall acknowledge the Bureau's participation in the research project.
    d. The research shall expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.
    e. Prior to submitting for publication the results of a research project conducted under this subpart, the researcher shall provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.
6. Other specific requirements of the DOJ Research Funded by the National Institute of Justice can be found in the "Additional Requirements for Department of Justice (DOJ) Research" section in the IRB's HRP-318 - WORKSHEET - Additional Federal Criteria.

Appendix A-7 Additional Requirements for Department of Education (ED) Research

1. Each school at which the research is conducted must provide an assurance that they comply with the Family Educational Rights and Privacy Act (FERPA) and the Protection of Pupil Rights Amendment (PPRA). Please see HRP-331- WORKSHEET- FERPA Compliance.
2. Provide a copy of all surveys and instructional material used in the research. Upon request parents of children[17] involved in the research[18] must be able to inspect these materials.
3. The school in which the research is being conducted must have policies regarding the administration of physical examinations or screenings that the school may administer to students.
4. Other specific requirements of the Department of Education (ED) Research can be found in the "Additional Requirements for Department of Education (ED) Research" section in the IRB's HRP-318 – WORKSHEET - Additional Federal Criteria.

[17] Children are persons enrolled in research not above the elementary or secondary education level, who have not reached the age or majority as determined under state law.

[18] Research or experimentation program or project means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.

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Appendix A-8 Additional Requirements for Veterans Administration (VA) Research

- VA research is research that is conducted by researchers (serving on VA compensated, WOC, or IPA appointments) while on VA time or on VA property. The research may be funded by VA, by other sponsors, or be unfunded. VA research must have Research and Development (R&D) Committee approval before it is considered VA Research and before it can be initiated. All research activities approved by the R&D Committee are considered VA Research.
    - VA-affiliated nonprofit research and education corporations (NPC) are authorized by Congress under 38 U.S.C. 7361-7366 to provide flexible funding mechanisms for the conduct of research and education at one or more VA facilities. Research approved by a facility R&D Committee are considered to be a VA research project or a VA education activity respectively, regardless of the source of funding, the entity administering the funds, or the research or education site (see VHA Handbook 1200.17, Department of Veterans Affairs Nonprofit Research and Education Corporations Authorized by Title 38 U.S.C. Sections 7361Through 7366, dated April 27, 2016 and revised May 9, 2017).
- VA research includes VA-approved research conducted at international sites not within the United States, its territories, or Commonwealths; and includes research where human tissues are sent outside the United States. The Investigator must give first priority to the protection of research subjects, uphold professional and ethical standards and practices, and adhere to all applicable VA and other federal requirements, including the local VA facility's and this institution's policies and procedures, regarding the conduct of research and the protection of human subjects. The Investigator must hold a current VA appointment to conduct VA research.
- The responsibilities of the Investigator may be defined in the protocol or IRB application. Specifically, the Investigator's responsibilities include, but are not limited to
    - Qualifications to Conduct Human Subjects Research. VA investigators must have the appropriate training, education, expertise, and credentials to conduct the research according to the research protocol.
        - Investigators must ensure that all research staff are qualified (e.g. including but not limited to appropriate training, education, expertise, and credentials) to perform procedures assigned to them during the course of the study.
        - Investigators and their staff conducting human subjects research must be credentialed and privileged as required by current local and VA requirements (see VHA Handbook 1100.19 and VHA Directive 2012-030, Credentialing of Health Care Professionals, or successor policy). Investigators and their research staff may only perform those activities in a research study for which they have the relevant credentials and privileges.
        - Investigators must be identified on the IRB application and must provide credentials, conflict of interest statements or other documentation required by VA and local facility policies.

- VHA Program Office employees acting as investigators, regardless of duty station, must prospectively document their research with their supervisor in writing.
- All individuals involved in conducting VA human subjects research are required to complete training in ethical principles on which human subjects research is to be conducted. Specific requirements regarding the type and frequency of training are found on ORD's Web site at: http://www.research.va.gov/pride/training/options.cfm. All other applicable VA and VHA training requirements at the local and national level must be met (e.g. privacy and information security training).

- Research Protocol. The Investigator must develop and submit a research protocol that is scientifically valid, describes the research objectives, background and methodology, and is relevant to the health or welfare of the Veteran population. When applicable, the protocol must include the following safety measures:
  - The type of safety information to be collected including AEs;
  - Frequency of safety data collection;
  - Frequency or periodicity of review of cumulative safety data;
  - Statistical tests for analyzing the safety data to determine if harm is occurring; and
  - Conditions that trigger an immediate suspension of the research, if applicable.
- Approvals. The Investigator must submit the protocol for initial review and obtain written approvals from the IRB, other applicable committees, and from the R&D Committee. In addition, the Investigator must receive written notice from the ACOS/R&D that the research may commence before initiating the research.
  - The Investigator may not self-certify that a study is exempt.
  - Once approved by the IRB, the protocol must be implemented as approved. All modifications to the approved research protocol or consent form must be approved by the IRB prior to initiating the changes except when necessary to eliminate apparent immediate hazards to the subject.
  - The Investigator must also obtain continuing review and approval at a frequency established by the IRB, but not less than once every year and is expected to submit all materials required for continuing review in sufficient time to assure approval prior to the expiration date. No research activities may be conducted at any time without a currently valid IRB approval.
- Conflict Of Interest. The Investigator must disclose to the IRB any potential, actual, apparent, or perceived conflict of interest of a financial, professional, or personal nature that may affect any aspect of the research, and comply with all applicable VA and other federal requirements regarding conflict of interest.
- Initial Contact. During the recruitment process, members of the research team must make initial contact with potential subjects in person or by letter prior to initiating any telephone contact, unless there is written documentation that the subject is willing to be contacted by telephone about the study in question or a specific kind of research as outlined in the study. (NOTE: This does not apply to situations where a Veteran calls in response to an advertisement. If existing information from sources such as a medical record or database (research or non-research) are used to identify human

subjects, there must be an IRB approved HIPAA waiver for this activity in the new protocol.)
    - Any initial contact by letter or telephone must provide a telephone number or other means that the potential subject can use to verify that the study constitutes VA research.
    - If a contractor makes the initial contact by letter, the VA Investigator must sign the letter.
- Informed Consent for Research. The Investigator must obtain and document legally effective informed consent of the subject or the subject's LAR prospectively (i.e. no screening or other interaction or intervention involving a human subject can occur until after the IRB-approved informed consent requirements have been met) that is in alignment with ethical principles that govern informed consent for research. The only exceptions are if the IRB determines the research is exempt, or approves a waiver of the informed consent process, or approves a waiver of the signed informed consent document.
    - If the Investigator does not personally obtain informed consent, the Investigator must delegate this responsibility in writing (e.g. by use of a delegation letter) to research staff sufficiently knowledgeable about the protocol and related concerns to answer questions from prospective subjects, and about the ethical basis of the informed consent process and protocol.
        - If the Investigator contracts with a firm (e.g. a survey research firm) to obtain consent from subjects, collect private individually identifiable information from human subjects, or are involved in activities that would engage that firm in human subjects research, the firm must have its own IRB oversight of the activity. In addition, the Privacy Officer must determine that there is appropriate authority to allow the disclosure of individual names and other information to the contracted firm.
        - The Investigator must ensure that all original signed and dated informed consent documents are maintained in the Investigator's research files, readily retrievable, and secure.
    - For exempt research activities involving the Investigator interacting with human subjects or obtaining information by educational tests, survey or interview procedures, or behavioral interventions, the following information must be given to the prospective human subject as applicable in writing or orally:
        - The activity is research;
        - Participation is voluntary;
        - Permission to participate can be withdrawn;
        - Permission for use of data can be withdrawn for exempt research activities involving the collection and use of identifiable data; and
        - Contact information for the VA Investigator.
- HIPAA Authorization. The Investigator or designee must obtain HIPAA authorization for the use and disclosure of the subject's PHI, or obtain an IRB-approved waiver of HIPAA authorization unless there is a limited data set and appropriate DUA. The written HIPAA authorization may either be a standalone

document or combined with the research informed consent approved by the IRB. If a standalone document is used as the written HIPAA authorization, VA Form 10-0493: Authorization for Use and Release of Individually Identifiable Health Information Collected for VHA Research must be used to document the authorization.

- Reporting. The Investigator is responsible for reporting problems, adverse events, local research deaths, and apparent serious or continuing non-compliance in accordance with local facility or IRB SOPs and VHA Handbook 1058.01.
  - VA personnel must ensure that the appropriate IRB of Record is notified, in writing, within five (5) business days after becoming aware of any apparent serious and/or continuing noncompliance with applicable laws, regulations, policies, and agreements pertaining to non-exempt human participants research. This includes, but is not limited to, serious or continuing noncompliance with the Common Rule, local VA medical facility policies and SOPs related to human participants research, if developed, IRB-approved protocols, and the requirements or determinations of the IRB.
  - In the event of a local research participant death, VA personnel must ensure that the appropriate IRB of Record is notified:
  - Immediately (i.e., within one hour) upon becoming aware of any local research death of a human participant that is believed to be both unexpected and related or possibly related to participating in a VA non-exempt human participant study. VA personnel must also provide follow-up written notification to the IRB within one (1) business day.
  - In the event of any apparent UPIRTSO, VA personnel must ensure that the appropriate IRB of Record is notified, in writing, within five (5) business days after becoming aware of any apparent UPIRTSO.

- Research Records. The Investigator is responsible for ensuring research records include all information made or received by a VA investigator over the entire lifecycle of a research activity. This includes, but is not limited to, as applicable, the research protocol and all amended versions of the protocol; the grant application; documentation on each subject including informed consent, interactions with subjects by telephone or in person, observations, interventions, and other data relevant to the research, codes and keys used to de-identify and re-identify subjects protected health information; documents related to budget and funding; and other forms required by VA policy and Federal regulations. If the Investigator leaves the VA, all research records must be retained for the applicable retention period by the VA facility where the research was approved. All records regardless of format (paper, electronic, electronic systems) must be managed per NARA approved records schedules found in VHA RCS 10-1 and therefore must be retained until disposition instructions, as approved by NARA, are published in VHA RCS 10-1. NOTE: Once the disposition schedule is determined, records should be disposed in accordance with VHA RCS 10-1.
  - VHA Health Record. A VHA health record must be created or updated, and a progress note created, for all research subjects (Veterans or non-Veterans) who receive research procedures or interventions as inpatients or outpatients at VA medical facilities that are either used in or may impact the medical care of the

research subject at a VA medical facility or at facilities contracted by VA to provide services to Veterans (e.g. Community-Based Outpatient Clinics or nursing homes) (see VHA Handbook 1907.01). Informed consent and HIPAA authorization documents are not required to be in the health record. The name and contact information of the researcher conducting the study should be included

- Investigational Drugs and Devices. The Investigator must conduct VA human subjects research involving investigational drugs and devices in accordance with all applicable VA policies and other federal requirements including, but not limited to: VHA Directive 1200.05, VHA Handbook 1108.04, Investigational Drugs and Supplies dated February 29, 2012, and applicable FDA regulations. The storage and security procedures for test articles used in research must be reviewed and approved by the IRB and follow all applicable federal rules.
- Initiation of Research Projects. IRB approval is for a specified time period based on the degree of risk of the study, not to exceed one (1) year except for research subject to the 2018 Requirements where continuing review is not required. The IRB determines the expiration date based upon its date of review and communicates that date to the Investigator in the written approval letter. The Investigator must not initiate the IRB approved research protocol until all applicable requirements in VHA Directive 1200.01 have also been met including obtaining R&D Committee approval and obtaining written notification from the ACOS/R&D that the research can be initiated.
- Expiration of IRB Approval. There is no provision for any grace period to extend the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur on or before the date when IRB approval expires. If approval expires, the Investigator must:
  - Stop all research activities including, but not limited to, enrollment of new subjects, analyses of individually identifiable data, and research interventions or interactions with currently participating subjects, except where stopping such interventions or interactions could be harmful to those subjects; and
  - Immediately submit to the IRB Chair a de-identified list of research subjects who could be harmed by stopping specified study interventions or interactions. The IRB Chair must determine within two (2) business days whether or not such interventions or interactions may continue.
- Documentation of Informed Consent
  - When documentation of informed consent is not waived by IRB, the Investigator or designee must ensure that the informed consent document is signed and dated by:
    - The subject or the subject's legally authorized representative.
  - If consent is obtained electronically, the following must be met:
    - Authentication controls on electronic consent provide reasonable assurance that such consent is rendered by the proper individual; and
    - The subject dates the consent as is typical or that the software provides the current date when signed.

- The following populations are considered categorically vulnerable and have specific VA requirements for their inclusion in research:
    - Fetuses. Research in which the focus is a fetus, either in-utero or ex-utero cannot be conducted by VA investigators while on official duty, at VA facilities, or at VA approved off-site facilities.
    - Neonates. Interventional research enrolling neonates cannot be conducted by VA investigators while on official duty, or at VA facilities, or at VA approved off-site facilities. Noninvasive monitoring involving minimal risk, prospective observational and retrospective record review studies that involve neonates or neonatal outcomes are permitted. See HRP-414 – CHECKLIST - Neonates of Uncertain Viability.
    - Pregnant Women. The VA medical facility Director must certify that the medical facility has sufficient expertise in women's or reproductive health to conduct the proposed research if the research includes interventional studies or invasive monitoring of pregnant women as subjects. See HRP-412 – CHECKLIST - Pregnant Women.
    - Prisoners. See HRP-415 – CHECKLIST - Prisoners.
    - Children. See HRP-416 - CHECKLIST - Children.
    - Subjects who Lack Decision-making Capacity. See HRP-417 - CHECKLIST - Cognitively Impaired Adults.
- Research Involving Prisoners
    - Research involving prisoners cannot be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities unless a waiver has been granted by the CRADO.
    - Waiver requests must be submitted electronically to the CRADO by the VA medical facility Director with the following documents:
        - A letter from the VA medical facility Director supporting the conduct of the VA study involving prisoners;
        - Rationale for conducting the research involving prisoners to include additional ethical protections taken by the proposed research for prisoners to make voluntary and uncoerced decisions whether or not to participate as subjects in research;
        - Documentation of the VA investigator's qualifications to conduct the research involving prisoners, such as a biosketch and a list of all research team members;
        - Location of businesses where the research is proposed to be conducted;
        - A copy of the IRB approval letter specifically documenting its review determinations according to 45 CFR 46.305(a);
        - A copy of the IRB minutes approving the research with documentation that at least one member of the IRB included a prisoner or a prisoner representative for the review of the research;
        - A copy of the IRB-approved research study;
        - A copy of the IRB-approved informed consent document; and
        - A copy of the written HIPAA authorization.
    - If such a waiver is granted, the research must comply with the requirements of 45 CFR 46.301 - 46.306.

- Research Involving Children
  - Research involving children must not present greater than minimal risk.
  - The VA medical facility Director must approve participation in the proposed research that includes children.
  - Research involving biological specimens or data obtained from children is considered to be research involving children even if de-identified. If the biological specimens or data were previously collected, they must have been collected under applicable policies and ethical guidelines.
  - The IRB must have the appropriate expertise to evaluate VA research involving children and must comply with the requirements of 45 CFR 46.401 - 46.404 and 46.408.
- Research Involving Persons Who Lack Decision-Making Capacity
  - The protocol must include a plan, that it is appropriate given the population and setting of the research, for how investigators will determine when a legally authorized representative will be required to provide informed consent. In general, the research staff must perform or obtain and document a clinical assessment of decision-making capacity for any subject suspected of lacking decision-making capacity.
  - When the potential subject is determined to lack decision-making capacity, investigators must obtain consent from the LAR of the subject (i.e. surrogate consent).
  - The following persons are authorized to consent on behalf of persons who lack decision-making capacity in the following order of priority:
    - Health care agent (i.e. an individual named by the subject in a Durable Power of Attorney for Health Care);
    - Legal guardian or special guardian;
    - Next of kin: a close relative of the patient 18 years of age or older, in the following priority: spouse, adult child, parent, adult sibling, adult relative;
    - Close friend; or
    - A clinical social worker licensed pursuant to Chapter 491, or who is a graduate of a court-approved guardianship program.
  - If feasible, the Investigator must explain the proposed research to the prospective research subject even when the legally authorized representative gives consent. Although unable to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may a subject be forced or coerced to participate in a research study even if the LAR has provided consent.
  - Legally authorized representatives must be told that their obligation is to try to determine what the subjects would do if able to make an informed decision. If the potential subjects' wishes cannot be determined, the legally authorized representatives must be told they are responsible for determining what is in the subjects' best interest.
- Research Involving Certificates of Confidentiality (CoC) (see HRP-333 – WORKSHEET - Certificate of Confidentiality)

- If information about the subject's participation will be included as part of the VHA medical record that information must be given to the prospective subject as part of the informed consent process that information regarding study participation will be included in the medical record.
- In instances where a written informed consent form is used, inclusion of a statement that the study has been issued a CoC is required.
- Investigators should work with the research office in their facility to assure that when Veterans are enrolled in a study protected by a Certificate of Confidentiality, they are not simultaneously enrolled in other interventional studies unless it is absolutely clear that this enrollment does not raise safety issues.

- Collaborative Research. This addresses collaborations between VA and non-VA investigators. Collaboration is encouraged when VA investigators have a substantive role in the design, conduct, and/or analysis of the research. VA may also serve as a Coordinating Center for collaborative studies.
  - IRB of Record Approval. Each institution is responsible for safeguarding the rights and welfare of human subjects and providing oversight of the research activities conducted at that institution.
    - Each collaborating institution engaged in human subjects research must obtain approval from its IRB of Record and hold a FWA or another assurance acceptable to VA (e.g. DOD assurance).
    - VA investigators must submit a protocol or other documentation to their VA IRB of Record that delineates which research activities will be conducted as the VA portion of the overall Collaborative Research study (e.g. by VA investigators on VA time or VA property).
    - Each institution engaged in the collaborative research must use the informed consent document and HIPAA authorization required by their respective institutional policies for subjects recruited from that institution, or procedures requiring participation of the subject at that institution. The informed consent document may contain information on the project as a whole as long as the document clearly describes which procedures will be performed under VA auspices and which will be performed under a non-VA institution's auspice.
      - The VA informed consent document must clearly state when procedures mentioned at other institutions are part of the VA's portion of the study.
      - The informed consent document and HIPAA authorization must not contain inconsistent provisions.
  - Waivers. PHI obtained in research for which the IRB of Record has waived the requirements to obtain a HIPAA authorization and a signed informed consent document may not be disclosed outside VA unless the VA facility Privacy Officer ensures and documents VA's authority to disclose the PHI to another institution. A waiver of HIPAA authorization is not sufficient to fulfill the requirements of other applicable privacy regulations such as the Privacy Act of 1974 (5 U.S.C. 552a).
  - Research Data. The protocol, addendum, and/or IRB of Record application must describe the data to be disclosed to collaborators, the entity(ies) to which the data are to be disclosed, and how the data are to be transmitted. This includes data from

individual subjects as well as other data developed during the research such as the analytic data and the aggregate data.
    - Each VA facility must retain a complete record of all data obtained during the VA portion of the research in accordance with privacy requirements, the Federal Records Act, and VHA Records Control Schedule (RCS) 10-1.
    - All disclosures and data transmission must meet privacy and security requirements per VA Directive 6500, VHA Handbook 6500, and VHA Handbook 1605.1.
    - Agreements regarding data use and transmission must be executed as required as applicable in VHA Handbook 1200.12, Use of Data and Data Repositories in VHA Research, dated March 9, 2009, or any superseding policies revising or replacing it.
- Photography, Video and/or Audio Recording for Research Purposes
    - The informed consent for research must include information describing any photographs, video, and/or audio recordings to be taken or obtained for research purposes, how the photographs, video, and/or audio will be used for the research, and whether the photographs, video, and/or audio will be disclosed outside the VA.
        - An informed consent to take a photograph, video, and/or audio recording cannot be waived by the IRB.
        - The consent for research does not give legal authority to disclose the photographs, video, and/or audio recordings outside the VA. A HIPAA authorization is needed to make such disclosures.
- International Research
    - VA international research is defined as any VA-approved research conducted at international sites (i.e. not within the United States (U.S.), its territories, or Commonwealths), any VA-approved research using either identifiable or de-identified human biological specimens or identifiable or de-identified human data originating from international sites, or any VA-approved research that entails sending such specimens or data out of the U.S. This definition applies regardless of the funding source (funded or unfunded) and to research conducted through any mechanism of support including MOUs, CRADAs, grants, contracts, or other agreements. NOTE: Research conducted at U.S. military bases, ships, or embassies is not considered international research.
        - Sending specimens or data to individuals with VA appointments at international sites (e.g. a WOC appointment, a VA investigator on sabbatical at an international site) is considered international research. Remote use of data that is maintained on VA computers within the U.S. or Puerto Rico and accessed via a secure connection is not considered international research.
        - International research includes multi-site trials involving non-U.S. sites where VA is the study sponsor, a VA investigator is the overall study-wide Investigator, VA holds the Investigational New Drug (IND), or the VA manages the data collection and the data analyses.
        - International research does not include studies in which VA is only one of multiple participating sites where the overall study-wide Investigator is not a VA

investigator (i.e. the Investigator for the study as a whole is not a VA investigator).

- Before approving international research involving human subjects research, the IRB must ensure that human subjects outside of the U.S. who participate in research projects in which VA is a collaborator receive equivalent protections as research subjects inside the U.S. (see OHRP guidance at http://www.hhs.gov/ohrp/international/index.html). NOTE: The VA medical facility Director must approve participation in the proposed international research.
- All international research must also be approved explicitly in a document signed by the VA medical facility Director, except for Cooperative Studies Program activities which must be approved by the CRADO.

- Use Preparatory to Research
  - VA investigators may use individually-identifiable health information to prepare a research protocol prior to submission of the protocol to the IRB for approval without obtaining a HIPAA authorization or waiver of authorization.
    - VA investigators must not arbitrarily review PHI based on their employee access to PHI until the Investigator documents the following required information as "Preparatory to Research" in a designated file that is readily accessible for those required to audit such information (e.g. Health Information Manager or Privacy Officer):
      - Access to PHI is only to prepare a protocol;
      - No PHI will be removed from the covered entity (i.e. VHA); and
      - Access to PHI is necessary for preparation of the research protocol.
    - Non-VA researchers may not obtain VA information for preparatory to research activities without appropriate VA approvals (see VHA Directive 1605.01).
    - During the preparatory to research activities the VA investigator:
      - Must only record aggregate data. The aggregate data may only be used for background information to justify the research or to show that there are adequate numbers of potential subjects to allow the Investigator to meet enrollment requirements for the research study;
      - Must not record any individually identifiable health information; and
      - Must not use any individually identifiable information to recruit research subjects.
      - Preparatory activities can include reviewing database output (computer file or printout) containing identifiable health information generated by the database owner, if the Investigator returns the database output to the database owner when finished aggregating the information.
    - Contacting potential research subjects and conducting pilot or feasibility studies are not considered activities preparatory to research.
    - Activities preparatory to research only encompass the time to prepare the protocol and ends when the protocol is submitted to the IRB.
- Posting of Clinical Trial Consent Forms. For studies subject to the 2018 Requirements, if a VA research study is a clinical trial, one IRB-approved informed consent form used to enroll subjects, unless the IRB waived documentation of informed consent, must be

posted by either the Investigator or the Federal department or agency conducting or supporting the study. The informed consent form must be posted after the clinical trial is closed to recruitment and no later than sixty (60) days after the last study visit by any subject as described in the IRB-approved protocol. For multi-site studies, it applies when the entire study has closed to subject recruitment. Any proprietary or personal information (such as names and phone numbers) must be redacted prior to posting the informed consent form.

  - For any ORD-funded clinical trial, the applicable ORD funding service will be responsible for posting the informed consent form.
  - For a clinical trial funded or supported by a Federal agency or department other than VA, the awardee is responsible for posting the informed consent form.
  - For a clinical trial funded or supported by a non-Federal agency or department (e.g. graduate school, industry, nonprofit organization) or not funded, the VA Investigator conducting the clinical trial is responsible for ensuring that the informed consent form is posted. If the clinical trial includes multiple sites engaged in the clinical trial, an agreement must exist specifying who is responsible for posting the informed consent form.

- Other specific requirements of Veterans Administration (VA) research can be found in the "Additional Requirements for Veterans Administration (VA) Research" section in the IRB's HRP-318 - WORKSHEET - Additional Federal Agency Criteria.

Appendix A-9 Single IRB Studies

1. That National Institutes of Health expects that all sites participating in multi-site studies involving non-exempt human subjects research funded by the NIH will use a single Institutional Review Board (sIRB) to conduct the ethical review required by the Department of Health and Human Services regulations for the Protection of Human Subjects at 45 CFR Part 46.
    a. This policy applies to the domestic sites of NIH-funded multi-site studies where each site will conduct the same protocol involving non-exempt human subjects research, whether supported through grants, cooperative agreements, contracts, or the NIH Intramural Research Program. It does not apply to career development, research training or fellowship awards.
    b. This policy applies to domestic awardees and participating domestic sites. Foreign sites participating in NIH-funded, multi-site studies will not be expected to follow this policy.
    c. Exceptions to the NIH policy will be made where review by the proposed sIRB would be prohibited by a federal, tribal, or state law, regulation, or policy. Requests for exceptions that are not based on a legal, regulatory, or policy requirement will be considered if there is a compelling justification for the exception. The NIH will determine whether to grant an exception following an assessment of the need.

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Appendix A-10 Additional Requirements for Research Subject to EU General Data Protection Regulations (GDPR)

1. Human subjects research involving personal data about individuals located in (but not necessarily citizens of) European Union member states, Norway, Iceland, Liechtenstein, and Switzerland is subject to EU General Data Protection Regulations.
2. For all prospective human subjects research subject to EU GDPR, contact institutional legal counsel or your institution's Data Protection Officer to ensure that the following elements of the research are consistent with institutional policies and interpretations of EU GDPR:
    a. Any applicable study design elements related to data security measures.
    b. Any applicable procedures related to the rights to access, rectification, and erasure of data.
    c. Procedures related to broad/unspecified future use consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens.
    d. Clinical Trial master file data must be kept for 25 years from study completion from all sites.
3. Where FDA or DHHS regulations apply in addition to EU GDPR regulations, ensure that procedures related to withdrawal from the research, as well as procedures for managing data and biospecimens associated with the research remain consistent with Appendices A-1 and A-2 above.

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Appendix A-11 Additional Requirements for Environmental Protection Agency (EPA) Research

1. Research conducted, supported, or intended to be submitted to EPA is subject to Environmental Protection Agency Regulations.
2. Intentional exposure of pregnant women or children to any substance is prohibited.
3. Observational research involving pregnant women and fetuses are subject to additional DHHS requirements for research involving pregnant women (45 CFR §46 Subpart B) and additional DHHS requirements for research involving children (45 CFR §46 Subpart D.)
4. Research involving children must meet category #1 or #2.
5. Other specific requirements of the Environmental Protection Agency (EPA) Research can be found in the "Additional Requirements for Environmental Protection Agency (EPA) Research and Research Intended to be Submitted to the Environmental Protection Agency" section in the IRB's HRP-318 - WORKSHEET - Additional Federal Agency Criteria.

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Appendix B-1 Summary of Manual Changes

Version	Date Approved (Date in document header)	Date Released	
7	3/1/2021	3/1/2021	-Clarified how to add participating sites. -Added the requirement for MGS researchers to use the approved MGS subject injury compensation and HIPAA language, as applicable. -Addition of procedures for dual enrollment. -Clarified where to find guidance related to CAPA plans and where to find deviation log templates. -Added information regarding sharing research results with subjects. -Clarified submission of RNIs for external submission. -Updated DOD requirements. -Updated DOE requirements. -Updated DOJ requirements.
8	5/16/2022	5/16/2022	-Minor sentence additions, deletions or changes throughout for improved clarity. - DNA Privacy language added to incorporate Florida Statutes §§ 760.40; 817.5644. - Added mor details on how to request MGS to serve as a single IRB of record (Questions # 9 and #29). - Additional information to clarify FERPA federal law when using student data for research. - Additional language to clarify when injury language is required. -Clarified several areas for PI reporting obligations after MGS IRB approval (Question #27). -Clarified Social Behavioral and Biomedical Serious Adverse Event reporting requirements (Question #28). - Moved all external IRB items (when MGS is Relying) to Question #30. - Minor clarifications about subject recruitment (Question #31). - More details provided about how to document consent (Question #32).

			- Clarified how and when to report protocol deviations or non-compliance with regulation, GCP or policy (Question #34). - Clarified how and when to submit a Continuing Review or annual Confirmation of Ongoing Research (Question #35). - Added more details about when a study can be closed (Question #36). - Updated how to request a non-affiliated person to assist in research, including adding the Individual Investigator Agreement (IIA) option, (Question #41).
9	4/6/23	4/7/23	- Revised appendix section "Additional Requirements for Department of Defense (DOD) Research" for consistency with AAHRPP's revised evaluation instrument. - Revised appendix section "Additional Requirements for Veterans Administration (VA) Research" to add a description of VA research and include VA requirements for notifying the IRB of Record of apparent serious and/or continuing noncompliance, death, or apparent UPIRTSO as noted in AAHRPP's revised Section C. - Added reference to HRP-318 for additional VA requirements. - Removed appendix section "COVID-19 Considerations for Investigators Conducting Human Research" as this is now addressed within Emergency Preparedness materials.
10			- Corrected formatting and typographical errors throughout. - Added statement to specify individuals required to disclose financial interest in research (Question #5) - Added reference to the Record Retention and Destruction guidance document (Question #11 and Question #37) - Added new policy/procedures related to Foreign Countries of Concern (Question #16) - Added clarification to applicability of the FL DNA Privacy Law (Question #17) - Added FL Statute for International Cultural Agreements (Question #17)

			- Additional considerations when determining compensation (Question #22) -Clarification on requirements when using an external IRB (Question #30) -Added statements clarifying what is allowed in medical record (Question #38). -Added information about assistance that QA/QI can offer (Question #38)