POLICY: Investigator Obligations

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1. PURPOSE

1.1. This policy describes the IRB's expectations of investigators conducting <Human Research> overseen by Aspire IRB, CGIRB, MLIRB, NEIRB, or WIRB.

1.2. For research overseen by an IRB other than Aspire IRB, CGIRB, MLIRB, NEIRB, or WIRB, investigators should follow the requirements of that IRB.

2. POLICY

2.1. Do not commence research until receipt of IRB approval and all other required approvals, such as radiation safety approval, biosafety approval, and approvals of departments or divisions that require approval of the use of their resources.

2.1.1. If there are any questions about whether you are conducting research involving human subjects, contact the IRB before commencing the study.

2.2. Comply with all requirements and determinations of the IRB.

2.3. 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.

2.4. 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.

2.5. Personally conduct or supervise the research.

2.6. Conduct the research in accordance with the relevant current protocol approved by the IRB.

2.7. Protect the rights, safety, and welfare of subjects involved in the research.

2.8. Submit proposed modifications to the IRB prior to their implementation.

2.8.1. Do not make modifications to the research without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to subjects.

2.9. Submit continuing reviews when requested by the IRB.

2.10. Submit a closure form to close research (end the IRB's oversight) when:

2.10.1. The protocol is permanently closed to enrollment

2.10.2. All subjects have completed all protocol related interventions and interactions

2.10.3. For research subject to federal oversight other than FDA:

2.10.3.1. No additional identifiable private information about the subjects is being obtained

2.10.3.2. Your analysis of private identifiable information is completed

2.11. If research approval expires, stop all research activities and immediately contact the IRB.

2.12. Promptly report to the IRB the information items listed in "POLICY: Prompt Reporting Requirements (HRP-071)."

2.13. Do not accept or provide payments to professionals in exchange for referrals of potential subjects ("finder's fees.")

2.14. Do not accept payments designed to accelerate recruitment that were tied to the rate or timing of enrollment ("bonus payments") without prior IRB approval.

2.15. For studies regulated by a federal department or agency, follow the additional obligations, as applicable:

2.15.1. "INVESTIGATOR GUIDANCE: Additional DOD Obligations (HRP-810)"

2.15.2. "INVESTIGATOR GUIDANCE: Additional DOE Obligations (HRP-811)"

2.15.3. "INVESTIGATOR GUIDANCE: Additional DOJ Obligations (HRP-812)"

2.15.4. "INVESTIGATOR GUIDANCE: Additional EPA Obligations (HRP-813)"

2.15.5. "INVESTIGATOR GUIDANCE: Additional ED Obligations (HRP-814)"

2.15.6. "INVESTIGATOR GUIDANCE: Additional FDA Obligations (HRP-815)"

2.16. For studies where ICH-GCP compliance is required, follow additional the obligations in "INVESTIGATOR GUIDANCE: Additional ICH-GCP Obligations (HRP-816)."
2.17. When required by the IRB ensure that consent, permission, and assent are obtained and documented in accordance with the relevant current protocol as approved by the IRB.
2.18. Retain research records (including signed consent documents) for the greater of:

2.18.1. Three years after completion of the research
2.18.2. For drug studies conducted under an IND, two 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 two years after the investigation is discontinued and FDA is notified.
2.18.3. For device studies conducted under an IDE or abbreviated IDE, two years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol.
2.18.4. The retention period required by the sponsor
2.18.5. The retention period required by local, state, or international law.

2.18.5.1. HIPAA requires signed authorizations to be retained for six years from the date signed or the date when it last was in effect, whichever is later.

2.18.6. The retention period required by a site that is not part of this [Organization].

3. REFERENCES

3.1. 21 CFR §50, §56
3.2. 45 CFR §46

4. REVISION HISTORY

4.1. **Edition 003:** Change "guidance" to "policy' and "obligations" to "IRB's expectations" in Purpose section.
4.2. **Edition 002.3:** Change identifier from HRP-800 to HRP-070 to categorize as a Policy, update reference of "HRP-801" to "HRP-071", and minor wording revision to 2.1.

POLICY: Prompt Reporting Requirements

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1. PURPOSE

1.1. This policy describes the information investigators must promptly report to the WCG IRB (Aspire IRB, CGIRB, HIRB, MLIRB, NEIRB, WIRB) overseeing the research.

1.2. For research overseen by an IRB other than a WCG IRB, investigators should follow the requirements of that IRB.

2. POLICY

2.1. Report the following information items to the IRB within 5 days:

2.1.1. New or increased risk[1]

2.1.2. Protocol deviation that harmed a subject or placed subject at risk of harm

2.1.3. Protocol deviation made without prior IRB approval to eliminate an immediate hazard to a subject

2.1.4. Audit, inspection, or inquiry by a federal agency

2.1.5. Written report or action of a government agency, regarding the research, the PI, or the research staff, or if research staff are added, a past history of such report or action, including:

2.1.5.1. Conviction of a crime

2.1.5.2. FDA Warning Letter

2.1.5.3. NIDPOE (Noticed of Initiation of Disqualification Proceedings and Opportunity to Explain)

2.1.5.4. Suspension or termination by an IRB

2.1.5.5. Suspension by a federal or governmental agency (such as FDA, HHS, or Health Canada)

2.1.5.6. OHRP Determination Letter, Health Canada Inspection Letter with observations, or similar

2.1.5.7. Form FDA 483 in the past 5 years

2.1.6. <Allegation of Noncompliance> or <Finding of Noncompliance>

2.1.7. Unauthorized disclosure of confidential information

2.1.8. Unresolved subject complaint

2.1.9. Suspension or premature termination by the sponsor, investigator, or institution

2.1.10. Incarceration of a subject in a research study not approved to involve prisoners

2.1.11. Adverse event or IND safety report that requires a protocol or consent change

2.1.12. State medical board or hospital medical staff actions, (denial, revocation, suspension, reduction, limitation, probation, non-renewal, relinquishment, sanction, fine, or discipline) regarding any of the following for the PI or research staff, or if research staff are added, a past history of such action:

2.1.12.1. Clinical privileges at any site

2.1.12.2. DEA licensure

2.1.12.3. Fellowship/board certification

2.1.12.4. Medical licensure in any state, nation, or province

2.1.12.5. Membership on any hospital staff

2.1.12.6. Prescribing privileges

2.1.12.7. Professional sanctions including fines and public reprimands

2.1.12.8. Professional society membership

2.1.12.9. Research privileges at any site

2.1.13. Unanticipated adverse device effect[2]

[1] For example, publications indicating a new risk, new risk in an investigator brochure, FDA black box warning, new risk identified in a data safety monitoring report, information or change that adversely affects subject safety, or information or change that adversely affects the conduct of the research.

2.1.14. Change in financial interest disclosure (submit as a modification)
2.1.15. Change in any other information previously submitted to the IRB (submit as a modification)

2.2. Information not listed above does not require prompt reporting to the [Organization's] IRB.

3. REFERENCES

3.1. 21 CFR §56.108(b)

4. REVISION HISTORY

4.1. **Edition 002:** Updated to align with reporting requirements listed on submission form and Promptly Reportable Information form.
4.2. **Edition 001.3:** Change identifier from HRP-801 to HRP-071 to categorize as a Policy and minor wording revision to 2.1.

[2] Unanticipated adverse device effect means 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.

1. PURPOSE

1.1. This guidance describes a process that in general is suitable to obtain informed consent.
1.2. Other procedures may be suitable when approved by the IRB.

2. BACKGROUND

2.1. "Person providing consent" means:

2.1.1. In the case of a cognitive intact adult, the individual being asked to take part
2.1.2. In the case of an adult unable to consent, that individual's LAR
2.1.3. In the case of a child:

2.1.3.1. One parent, if the other parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
2.1.3.2. One parent if the IRB determined that permission from one parent was sufficient
2.1.3.3. An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care
2.1.3.4. Both parents

2.2. "Consent information" means:

2.2.1. Long form consent document (when the IRB requires the long form of consent documentation)
2.2.2. Short form consent document and summary (when the IRB allows the short form of consent documentation)
2.2.3. Script or information sheet (when the IRB has approved a waiver of documentation of consent)

2.3. Communicate in the preferred language of the person providing consent
2.4. Unless the IRB affirmatively approved a protocol to include the following populations, such subjects may not be enrolled:

2.4.1. Adults unable to consent
2.4.2. Children
2.4.3. Neonates of uncertain viability
2.4.4. Nonviable neonates
2.4.5. Pregnant women
2.4.6. Prisoners
2.4.7. Individuals unable to speak English

2.5. The short form of consent documentation may be use only if affirmatively approved by the IRB.
2.6. For the short form of consent documentation:

2.6.1. The short form is a standard template translated into the subject's language.
2.6.2. The summary is the English version of the long form.

2.7. For waiver of documentation of consent, the script is the long form without a signature block.
2.8. Interpreters are to be conversant in both English and the language understood by the person providing consent. When allowed by institutional policy, the interpreter may be a member of the research team, or a family member or friend of the subject or person providing consent.
2.9. If the consent process requires an <Impartial Witness>:

2.9.1. The <Impartial Witness> is to be present during the entire consent discussion and to attest that the information in the consent form and any other information

provided was accurately explained to, and apparently understood by, the subject/LAR, and that consent was freely given.

2.9.2. The <Impartial Witness> may not be a person involved in the research.

3. GUIDANCE

3.1. Obtain the IRB-approved consent document, short form consent document, or script, as applicable.

3.1.1. Verify that you are using the most current IRB-approved information.

3.1.2. Verify that the consent document, if any, is in language understandable to the person providing consent.

3.2. If the person providing consent cannot read or the short form of consent documentation is used, obtain an <Impartial Witness>.

3.3. If the person providing consent cannot speak English, obtain the services of an interpreter.

3.4. Go over the information in the consent document using language understandable to the person providing consent.

3.4.1. Do not provide any information to the person providing consent through which the person providing consent is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

3.4.2. When providing information about treatments or compensation for injury, provide factual information and avoid statements that imply that compensation or treatment is never available.

3.5. Invite and answer questions.

3.6. Evaluate whether the following is true for the person providing consent. If not, take steps to correct or determine that the person providing consent is incapable of providing consent:

3.6.1. The person providing consent has been provided sufficient information.

3.6.2. The person providing consent understands the information

3.6.2.1. If the person providing consent has a disease or condition that may affect cognition, assess whether the person providing consent has sufficient cognitive capacity to legally provide informed consent.

3.6.2.2. If the subject is pregnant, ensure the person providing consent is fully informed regarding the reasonably foreseeable effect of the research on the fetus or neonate.

3.6.3. The person providing consent does not feel coerced or unduly influenced.

3.6.3.1. Ensure there is no threat of harm or adverse consequences for a decision to not participate.

3.6.3.2. Ensure that outside parties (family or caretakers) do not coerce or unduly influence the person providing consent, especially if that person is vulnerable to coercion or undue influence.

3.6.3.3. Ensure that the amount of payment does not coerce or unduly influence economically disadvantaged individuals.

3.6.3.4. For persons providing consent who are in a subordinate position to a member of the research team (e.g., employee or student), ensure that there is no threat of harm or adverse consequences to the subject's position for a decision to not participate.

3.6.4. The person providing consent has sufficient time to make a decision.

3.6.4.1. Provide the person providing consent with sufficient time to understand the information. Spend as much time as needed

3.6.4.2. Provide the person providing consent with sufficient time to ask questions.

3.6.5. The individual providing consent understands the consequences of a decision.
3.6.6. The individual providing consent can communicate a choice.

3.7. Once a person providing consent indicates that he or she does not want to consent, stop.
3.8. If the subject is a child or adult unable to consent:

3.8.1. Explain the research to the extent compatible with the subject's understanding.

3.8.1.1. Ensure that parents or guardians do not coerce or unduly influence children.
3.8.1.2. Ensure that outside parties (family or caretakers) do not coerce or unduly influence adults unable to consent.

3.8.2. If the IRB determined that assent was a requirement and the subject is capable of being consulted, request the assent (affirmative agreement) of the subject.

3.8.2.1. If the subject indicates that he or she does not want to take part, stop.

4. REFERENCES

4.1. 21 CFR §50.20, §50.25
4.2. 45 CFR §46.116

5. REVISION HISTORY

5.1. **Edition 002.4:** Triennial review - no changes
5.2. **Edition 002.3:** Update logo and footer

1. PURPOSE

1.1. This guidance describes a process that in general is suitable to document consent in writing.
1.2. Other procedures may be suitable when approved by the IRB.

2. BACKGROUND

2.1. "Person providing consent" means:

2.1.1. In the case of a cognitive intact adult, the individual being asked to take part
2.1.2. In the case of an adult unable to consent, that individual's LAR
2.1.3. In the case of a child:

2.1.3.1. One parent, if the other parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
2.1.3.2. One parent if the IRB determined that permission from one parent was sufficient
2.1.3.3. An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care
2.1.3.4. Both parents

2.2. The short form of consent documentation may be use only if affirmatively approved by the IRB.
2.3. For the short form of consent documentation:

2.3.1. The short form is a standard template translated into the subject's language.
2.3.2. The summary is the English version of the long form.

2.4. If the consent process required an <Impartial Witness>:

2.4.1. The <Impartial Witness> is to be present during the entire consent discussion and to attest that the information in the consent form and any other information provided was accurately explained to, and apparently understood by, the subject/LAR, and that consent was freely given.
2.4.2. The <Impartial Witness> may not be a person involved in the research.

3. GUIDANCE

3.1. If the consent process will be documented with the long form:

3.1.1. Verify that the document is in language understandable to the person providing consent.
3.1.2. If the IRB required written documentation of assent, note one of the following:

3.1.2.1. Assent of the child was obtained.
3.1.2.2. Assent of the child was not obtained because the capability of the child is so limited that the child cannot reasonably be consulted.

3.1.3. Have the following individuals personally sign and date the consent document:

3.1.3.1. Person giving consent
3.1.3.2. Person obtaining consent
3.1.3.3. <Impartial Witness>, if any

3.2. If the consent process will be documented with the short form:

3.2.1. Verify that the document is in language understandable to the person providing consent.
3.2.2. If the IRB required written documentation of assent, note one of the following:

3.2.2.1. Assent of the child was obtained.
3.2.2.2. Assent of the child was not obtained because the capability of the child is so limited that the child cannot reasonably be consulted.

3.2.3. Have the following individuals personally sign and date the consent document:

3.2.3.1. Person giving consent
3.2.3.2. Person obtaining consent
3.2.3.3. <Impartial Witness>

3.2.4. Have the following individuals personally sign and date the summary:

3.2.4.1. Person giving consent
3.2.4.2. Person obtaining consent
3.2.4.3. <Impartial Witness>

3.3. Provide the person providing consent with copies of the signed and dated documents.

3.3.1. This may be accomplished either by making a photocopy or by having individuals sign and date two copies.

3.4. File a copy of the consent document with the medical record when required by local policy.
3.5. Retain the signed and dated documents in the study records for the greater of:

3.5.1. Three years after completion of the research
3.5.2. For drug studies conducted under an IND, two 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 two years after the investigation is discontinued and FDA is notified.
3.5.3. For device studies conducted under an IDE or abbreviated IDE, two years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol.
3.5.4. The retention period requested by the sponsor.
3.5.5. The retention period required by local, state, or international law.
3.5.6. The retention period required by a site that is not part of this [Organization].

4. REFERENCES

4.1. 21 CFR §50.27, 56.115(b), §312.62(c), §812.140(d)
4.2. 45 CFR §46.115(b), §46.117

5. REVISION HISTORY

5.1. **Edition 001.2:** Triennial review - no changes
5.2. **Edition 001.1:** Update logo and footer

1. PURPOSE

1.1. This guidance outlines the additional obligations of investigators conducting research supported or conducted by DOD.

2. GUIDANCE

2.1. The following activities conducted or supported by the DoD are not considered human subject research:

2.1.1. Activities carried out solely for purposes of diagnosis, treatment, or prevention of injury and disease under force health protection programs of DoD, including health surveillance pursuant to Section 1074f of Title 10, U.S.C., and the use of medical products consistent with DoDI 6200.02.

2.1.2. Health and medical activities as part of the reasonable practice of medicine or other health professions undertaken for the sole purpose of diagnosis, cure, mitigation, treatment, or prevention of disease in a patient.

2.1.3. Activities performed for the sole purpose of medical quality assurance (see Section 1102 of Title 10, U.S.C., and DoDI 6025.13).

2.1.4. Activities that meet the definition of operational test and evaluation as defined in Section 139(a)(2)(A) of Title 10, U.S.C.

2.1.5. Activities performed solely for assessing compliance, including occupational drug testing, occupational health and safety reviews, network monitoring, and monitoring for compliance with requirements for protection of classified information.

2.1.6. Activities, including program evaluation and surveys, user surveys, outcome reviews, and other methods, designed solely to assess the performance of DoD programs where the results are only for the use of government officials responsible for the operation or oversight of the program being evaluated.

2.2. This guidance applies to:

2.2.1. OSD, the Military Departments, the Office of the Chairman of the Joint Chiefs of Staff and the Joint Staff, the Combatant Commands, the Office of the Inspector General of the Department of Defense, the Defense Agencies, the DOD Field Activities, and all other organizational entities within the DOD (referred to collectively in this issuance as the “DOD Components”).

2.2.2. DOD Components and other organizational entities that issue, implement, update, and monitor a component human research protection program (HRPP) management plan (component human research protection program management plan) in order to conduct or support DOD research involving human subjects, such as the Defense Health Agency, the National Security Agency, the Defense Intelligence Agency, the DOD Human Resources Activity, the DOD Educational Activity, the Uniformed Services University of the Health Sciences, the Defense Acquisition University, the National Defense University, and the Special Operations Command.

2.2.3. Human subject research (human subject research) conducted or supported by the DOD (for DOD exclusions, see Glossary).

2.2.4. Activities conducted or supported by the DOD, such as research, development, testing, and evaluation that involve humans, human data, human biospecimens, or activities regulated by the Food and Drug Administration (FDA).

2.3. This guidance’s applicability is not dependent upon the budget activities funding the research, the security classification of the research, the location of the research in the United States or a foreign country, or whether the research is conducted or supported by a program that is not considered research for other purposes. Guidance regarding this issuance is available on the Under Secretary of Defense for Research and Engineering (Under

Secretary of Defense for Research and Engineering DOD Office for Human Research Protections (DOD Office for Human Research Protections) website https://rt.cto.mil/ddre-rt/dd-rtl/hsd/hrp/.

2.4. The DOD will:

2.4.1. Follow Part 219 of Title 32, CFR, and the Belmont Report (44 Federal Register 23192, April 18, 1979) principles, including respect for persons, beneficence, and justice.

2.4.2. Recognize that certain categories of human research subjects are vulnerable populations, in accordance with Subparts B, C, and D in Part 46 of Title 45, CFR, who are thus afforded additional protections, as specified in this issuance.

2.4.3. Recognize and adhere to Subpart E in Part 46 of Title 45, CFR.

2.4.4. Prohibit human subject research for the testing of chemical or biological agents, pursuant to Section 1520a of Title 50, United States Code (U.S.C.). Some exceptions for research for prophylactic, protective, or other peaceful purposes apply. Before any excepted testing of chemical or biological agents involving human subject research can begin, the DOD Component seeking to conduct the human subject research must receive explicit written approval from the DOD Office for Human Research Protections. The DOD Office for Human Research Protections will send a copy of the protocol and approvals for such research to the Assistant Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs or any successor office.

2.4.5. Comply with all applicable biosafety and biosecurity requirements for activities conducted pursuant to this issuance; for example: DOD 6055.18-M, the current editions of Centers for Disease Control and Prevention, “Biosafety in Microbiological and Biomedical Laboratories (BMBL),” and the National Institutes of Health guidelines for research involving recombinant or synthetic nucleic acid molecules.

2.4.6. Conduct and support human subject research outside of the United States in accordance with federal and DOD regulatory requirements and the host nation’s laws, as applicable. Host nation human subject research laws are not typically applicable to DOD-conducted research that only involves DOD-affiliated personnel as research subjects. In cases when a DOD-affiliated person who is also a citizen of the host nation is a research subject, however, it is more likely that the host nation’s human subject research laws will be applicable. DOD Components conducting and supporting human subject research outside of the United States will consult with legal counsel, on a case-by-case basis, to determine whether host nation human subject research laws are applicable. Where differences in applicable standards exist, the standard that is most protective of human subjects will be applied.

2.4.7. Require the key investigator to provide written notification to the U.S. Central, U.S. Africa, U.S. European, U.S. Indo-Pacific, and U.S. Southern Commands of human subject research that is to be conducted or supported in their area of responsibility before human subject research proceeds. This does not apply to research performed within the United States or at DOD institutions overseas.

2.4.8. Require research involving large-scale genomic data (large-scale genomic data) collected from DOD-affiliated personnel to be subject to DOD Component security review and DOD Office for Human Research Protections approval, including the secondary use or sharing of de-identified data or specimens.

2.4.9. Permit the use of broad consent, in accordance with Part 219 of Title 32, CFR, in DOD-supported research. DOD will permit use of broad consent in DOD-conducted and collaborative research pursuant to DOD Office for Human Research Protections guidance and with DOD Component notification to the DOD Office for Human Research Protections that a DOD institution intends to use broad consent in a research protocol.

2.4.10. Require use of a single institutional review board (IRB) in accordance with Section 219.114 of Title 32, CFR. If a DOD institution believes that the research is not subject to the provision listed in Section 219.114(b) of Title 32, CFR, the applicable DOD Component Office of Human Research Protections (component human research protection program management plan) may determine and document, in accordance with Section 219.114(b)(2)(ii) of Title 32, CFR, that use of a single IRB is not appropriate for the particular context of the proposed human subject research. Studies already in progress before January 20, 2020, will not be required to transition to a single IRB, nor submit exception documentation.

2.4.11. Recognize that component human research protection program management plans have the authority to determine appropriate redactions when posting informed consent forms pursuant to Part 219 of Title 32, CFR, as presented by DOD institutions under their purview.

2.4.12. Recognize that certain activities subject to this issuance are excluded from the requirements outlined in DOD Instruction (DOD instruction) 8910.01, Volumes 1 and 2 of DOD Manual 8910.01, and DOD instruction 1100.13. These include public or internal information collections of facts or opinions, obtained initially or in follow-up requests, from individuals (including individuals in control groups) under treatment or clinical examination in connection with research on, or prophylaxis to prevent, a clinical disorder; direct treatment of that disorder; or the interpretation of biological analyses of body fluids, tissues, or other specimens; or the identification or classification of such specimens. These issuances may include other exclusions.

2.5. Under Secretary of Defense for Research and Engineering

2.5.1. Is the:

2.5.1.1. DOD point of contact for all matters related to DOD compliance with this issuance.

2.5.1.2. Principal DOD liaison with agencies and organizations outside the DOD on matters pertaining to human subject research, including ethics and privacy concerns in research as they relate to human subject research.

2.5.2. Provides procedures and guidance necessary to implement this issuance.

2.5.3. Exercises:

2.5.3.1. The authorities of:

2.5.3.1.1. The department head identified in Part 219 of Title 32, CFR.

2.5.3.1.2. The Secretary of Defense identified in Section 980 of Title 10, U.S.C.

2.5.3.1.3. The Secretary of Defense for Subparts B-E of Part 46 of Title 45, CFR.

2.5.3.2. The authority, direction, and control of the DOD Office for Human Research Protections to:

2.5.3.2.1. Halt studies and rescind or limit authorities granted to DOD Components' HRPPs, as needed.

2.5.3.2.2. Accept and approve each DOD Component's component human research protection program management plan, implementing and supporting policies or any modifications thereto, and provide oversight of the plan's implementation for compliance with this issuance. A DOD Office for Human Research Protections-approved component human research protection program management plan must be in place before DOD Components conduct or support any research involving human participants. The direct oversight

of the DOD Component's implementation of its component human research protection program management plan and subsequent HRPP is with the DOD Office for Human Research Protections.

2.5.3.2.3. Establish guidance for:

2.5.3.2.3.1. DOD Component human subject protection training.

2.5.3.2.3.2. DOD Component security review of research involving large-scale genomic data collected on DOD-affiliated personnel, to include administrative, technical, and physical safeguards for protecting their confidentiality both during and after the conduction of research.

2.5.3.2.3.3. DOD Component review of the ethical, legal, and social implications of emerging, readily available technologies or controversial research, development, testing, and evaluation.

2.5.3.2.3.4. Mandatory submittal document for all DOD-supported human subject research.

2.5.3.2.4. Performance of site visits to and inspections of DOD and non-DOD institutions that conduct research, or receive DOD support, as applicable, with or without prior notice.

2.5.4. Grants exceptions, consistent with law, to requirements in this issuance based on a written, appropriate justification from the senior designated official (senior designated official).

2.5.5. Delegates DOD Office for Human Research Protections authorities as appropriate.

2.5.6. Provides procedures in accordance with this issuance for use of certificates of confidentiality.

2.5.7. Designates DOD representatives to federal committees as appropriate.

2.5.8. Establishes and coordinates the activities of the DOD Coordinating Committee for HRPPs (Coordinating Committee for Human Research Protection Programs), along with its Executive Secretariat, the DOD Office for Human Research Protections Cabinet (DOD Office for Human Research Protections Cabinet). The DOD Office for Human Research Protections Cabinet is the central advisory body to the DOD, Under Secretary of Defense for Research and Engineering, and the DOD Office for Human Research Protections on matters outlined in this issuance.

2.5.9. Conducts Component HRPP assessments every other year.

2.5.10. Maintains:

2.5.10.1. A list of classified human subject research.

2.5.10.2. Lists of DOD IRBs and DOD Institutional Biosafety Committees.

2.5.11. Designates:

2.5.11.1. The Director, Human Systems Directorate, who chairs the Coordinating Committee for Human Research Protection Programs and oversees the Director, DOD Office for Human Research Protections.

2.5.11.2. The Director, DOD Office for Human Research Protections the authority for the operations of the DOD Office for Human Research Protections, and the designated manager for this issuance.

2.6. The heads of DOD Components that conduct or support human subject research:

2.6.1. Issue, implement, update, and monitor the component human research protection program management plan for implementing this issuance and guidance or memoranda pursuant to this issuance.

2.6.2. Identify the senior designated official, who will either hold the rank of general officer/flag officer or be a member of the Senior Executive Service, and will have the authority to implement the component human research protection program management plan.

2.6.3. Establish a component human research protection program management plan with authority and responsibility for the component human research protection program management plan and regulatory oversight of Component human subject research at its office and its institutions.

2.6.4. Provide well-qualified, experienced staff and sufficient resources commensurate with the Component's research portfolio, appointing at least a GS-15 or equivalent federal employee to direct the component human research protection program management plan and subsequent HRPP. This individual's experience in DOD-conducted and DOD-supported human subject research, staff management, and systems of record must be commensurate with the scope of the HRPP.

2.6.5. Provide members to intra- and interagency committees, the Coordinating Committee for Human Research Protection Programs, and the DOD Office for Human Research Protections Cabinet when requested.

2.6.6. Require that all Component institutions and sub-institutions that conduct or support human subject research have a Component-approved HRPP.

2.6.7. Provide an index of all DOD-conducted or DOD-supported human subject research to the DOD Office for Human Research Protections before the end of each fiscal year.

2.7. The senior designated official of a DOD Component that conducts or supports human subject research:

2.7.1. Will provide to the DOD Office for Human Research Protections, through the component human research protection program management plan, copies of human subject protections-related substantive communications or reports provided to the White House, federal courts, the FDA, congressional staff, committees, or State or local representatives within 5 business days after learning of the communications or reports.

2.7.2. Will provide to the DOD Office for Human Research Protections, through the component human research protection program management plan, copies of waivers to this issuance granted to a component human research protection program management plan on behalf of the senior designated official, if given the authority by the DOD Office for Human Research Protections, within 5 business days of issuing the waiver. This reporting requirement does not apply to waivers as described throughout Part 219 of Title 32, CFR, issued by institutional officials (IOs) or IRBs (i.e., waivers of documentation of informed consent or waivers of informed consent).

2.7.3. Will provide to the DOD Office for Human Research Protections, through the component human research protection program management plan, approvals and documentation of human subject research in fetal research as described in Sections 289g–289g-2 of Title 42, U.S.C. The senior designated official must obtain written approval from the DOD Office for Human Research Protections before human subject research activities involving fetal research may begin.

2.7.4. Will provide to the DOD Office for Human Research Protections, through the component office of human research protections, approvals and documentation of protocols requiring certification from the senior designated official that the reviewing IRB has fulfilled its duties in accordance with Subpart B of Part 46 of Title 45, CFR, for research that would not otherwise be approved but for the fact that it presents an opportunity to understand, prevent, or alleviate a serious

problem affecting the health or welfare of pregnant women, fetuses, or neonates. The senior designated official must obtain written approval from the DOD Office for Human Research Protections before permitting any human subject research to be conducted that involves research that would not otherwise be approved but for the fact that it presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates.

2.7.5. Will provide to the DOD Office for Human Research Protections, through the component human research protection program management plan, approvals of human subject research requiring a waiver to Section 512 of the E-Government Act of 2002 (Public Law 107-347), and the notice to the Office of Management and Budget, pursuant to the E-Government Act of 2002 and Pages 33362-33377 in Volume 72, Federal Register, within 5 business days of approving the human subject research.

2.7.6. Will provide to the DOD Office for Human Research Protections, through the component human research protection program management plan, reports of for-cause audits, reviews, or assessments conducted by or on behalf of the component human research protection program management plan within 5 business days of writing the document.

2.7.7. Will provide to the DOD Office for Human Research Protections, through the component human research protection program management plan, reports of audits of DOD-conducted or DOD-supported human subject research by another federal or State agency, official governing body of a Native American or Alaskan native tribe, other official entity, or foreign government, within 5 business days of discovering that such audit reports exist.

2.7.8. Will provide to the DOD Office for Human Research Protections, through the component human research protection program management plan, reports required in accordance with Title 32, CFR, or similar reports upon request by the DOD Office for Human Research Protections, within 5 business days of the report's completion, pertaining to:

2.7.8.1. Allegations of serious or continuing noncompliance related to human subject research that are substantiated by investigation, and subsequent actions taken based on the findings;

2.7.8.2. Unanticipated problems involving risks to human subjects or others and subsequent actions taken based on the findings; or

2.7.8.3. Suspensions or terminations of IRB approval.

2.7.9. Will submit written justification to the DOD Office for Human Research Protections to establish a new IRB, or substantially modify an IRB, at a minimum of 120 business days before establishment or modification for DOD Office for Human Research Protections concurrence. Will notify the DOD Office for Human Research Protections at least 120 business days before disestablishing an IRB.

2.7.10. Will provide details of DOD Component security reviews too the DOD Office for Human Research Protections, no fewer than 30 business days before beginning research involving large-scale genomic data collected from DOD-affiliated personnel.

2.8. component human research protection program management plan

2.8.1. The component human research protection program management plan must:

2.8.1.1. Include or reference DOD Component policies to implement this issuance and identify the responsible DOD Component office(s) for actions identified in this issuance.

2.8.1.2. Identify the senior designated official with the authority and responsibility for implementing the component human research protection program management plan.

2.8.1.3. Be consistent with DOD Office for Human Research Protections guidance and include or reference DOD Component policies and procedures, if applicable, that:

2.8.1.3.1. Establish authority for, and include or reference policies under which, the component human research protection program management plan will issue, limit, or revoke DOD assurances upon assessment of institutions' HRPPs.

2.8.1.3.2. Describe the DOD Component's program or provisions for exercising authorities delegated from the DOD Office for Human Research Protections to the senior designated official.

2.8.1.3.3. Describe, consistent with DOD Office for Human Research Protections guidance, the DOD Component's implementation of security review of research involving large-scale genomic data collected from DOD-affiliated personnel and procedures to obtain senior designated official and DOD Office for Human Research Protections approval.

2.8.1.3.4. Establish DOD Component and institutional requirements for human subject protection training.

2.8.1.3.5. Establish procedures for certification in accordance with Part 219 of Title 32, CFR.

2.8.1.3.6. Establish policy for designating human protections directors (human protections directors), human research protection official(s) (human research protection officials) and exemption determination officials to include specifying qualifications, training, and responsibilities.

2.8.1.3.7. Establish policy and institutional requirements for managing allegations of, and reporting noncompliance with, federal regulations, State and local laws, Native American or Alaskan native tribal laws, foreign laws, and DOD issuances and policies.

2.8.1.3.8. Establish DOD Component and institutional responsibilities for required reporting to the DOD Office for Human Research Protections, including reports pursuant to Title 32, CFR.

2.8.1.3.9. Establish policy and institutional requirements for managing conflicts of interest, including financial and non-financial interest conflicts, personal considerations, or perceptions of a possible conflict.

2.8.1.3.10. Establish policy for the maintenance of human subject research records, including records and workflows maintained in electronic form, required by governing regulations and this issuance.

2.8.1.3.11. Establish policy in accordance with DOD instruction 6025.23 for addressing subjects' research-related injuries in DOD-conducted research.

2.8.1.3.12. Establish policy and institutional requirements for human research protection official review of DOD-supported human subject research conducted by non-DOD institutions.

2.8.1.3.13. Establish policy and institutional requirements for administrative review of DOD-supported and DOD-conducted human subject research performed by DOD and non-DOD institutions.

2.8.2. Required component human research protection program management plan elements may be modified upon waiver request by the component human research protection program management plan or the prospective component human research protection program management plan on behalf of the senior designated official for DOD Office for Human Research Protections approval.

2.8.3. A DOD Component may, in a written arrangement approved by the DOD Office for Human Research Protections, rely on another DOD Component to implement elements of the relying DOD Component's component human research protection program management plan, except for designating the relying DOD Component's senior designated official. The DOD Component relying on another DOD Component to implement elements of its component human research protection program management plan must specify the existence and extent of any such reliance in its component human research protection program management plan.

2.9. Under the authority, direction, and control of the senior designated official in the DOD Component, each commander or director of a DOD institution that conducts or supports human subject research must:

2.9.1. Establish, implement, and maintain an HRPP to ensure the institution's compliance with this issuance.

2.9.2. Provide experienced, well-qualified HRPP staff and appropriate resources needed to ensure compliance with this issuance.

2.9.3. Designate a human protections director as the primary point of contact for the institution's HRPP.

2.9.4. As applicable, identify an IO to establish and maintain a DOD assurance and other appropriate assurances. An alternate IO (Alternate Institutional Official) may be appointed.

2.9.5. Evaluate and improve the institution's HRPP, its policies, and its standard operating procedures.

2.9.6. Establish a program of post-approval compliance monitoring of human subject research conducted or supported by the institution.

2.10. FEDERAL ASSURANCE.

2.10.1. When a Federal Assurance Is Required.

2.10.1.1. A DOD institution conducting non-exempt human subject research must have a DOD assurance for the protection of human subjects. All DOD assurances must be executed using templates approved by the DOD Office for Human Research Protections. Regional or multi-site DOD assurances are allowed as long as they are reasonable and can be overseen adequately; these must be approved by the DOD Office for Human Research Protections.

2.10.1.2. A DOD institution must have a Department of Health and Human Services (HHS) assurance, also known as a federal-wide assurance (FWA), when conducting non-exempt human subject research supported by HHS.

2.10.1.3. A non-DOD institution must rely on an FWA, or a comparable federal assurance, when engaged in non-exempt DOD-supported human subject research.

2.10.1.4. Researchers affiliated with institutions that do not hold a federal assurance may enter into individual investigator agreements (individual investigator agreement) to associate with an institution with a federal assurance. All researchers conducting non-exempt human subject research must be covered by their own institution's federal assurance or by another institution's federal assurance through an individual investigator agreement.

2.10.1.5. All institutions with a DOD assurance must identify at least one IRB on their DOD assurance, and must list all DOD IRBs operated by their institution, as well as agreements for IRB support.

2.10.1.6. An institution with a DOD assurance must, on its assurance(s), identify the IO as the senior individual authorized to represent the institution; establish and be responsible for the institution's HRPP; and identify the human protections director as the primary contact for the institution's HRPP.

2.10.1.7. DOD institutions and all non-DOD institutions conducting human subject research that receive support from the DOD must comply with the terms of their federal assurances, if they hold one, this issuance, and relevant policies of the cognizant DOD Component.

2.10.2. When a Federal Assurance Is Not Required.

2.10.2.1. A federal assurance is not required when an institution's role is limited to the conduct or support of exempt human subject research or activities determined by designated HRPP personnel to be research not involving human subjects.

2.10.2.2. DOD institutions that only support human subject research conducted by an institution with an assurance, also known as an assured institution, are not required to maintain their own federal assurance.

2.11. DOD-CONDUCTED RESEARCH.

2.11.1. DOD Institutional Approval and Oversight.

2.11.1.1. DOD institutions must have policies and procedures to ensure that all applicable human subject research approvals are in place before human subject research begins.

2.11.1.2. A DOD IO or Alternate Institutional Official, on behalf of their institution, may enter into an agreement to rely on another DOD institution's IRB without executing an Institutional Agreement for IRB Review (IAIR) because both institutions rely on DOD assurances that delineate the responsibilities of the reviewing and relying DOD IRBs.

2.11.1.3. A DOD IO or Alternate Institutional Official, on behalf of their institution, may establish an agreement for IRB support with an institution that does not hold a federal assurance. This agreement is not an IAIR; rather it is an agreement between an assured institution and a non-assured institution providing IRB services. The agreement must specify that the IRB must apply the requirements in this issuance for DOD-conducted research. The DOD IO and Alternate Institutional Official must be given approval by the component human research protection program management plan, on behalf of the senior designated official, to have the ability to establish such agreements.

2.11.1.4. DOD IRBs must comply with Section 219.107 of Title 32, CFR.

2.11.1.5. DOD IRBs will document their consideration of scientific merit; within the consideration of scientific merit, feasibility of study completion should be considered.

2.11.1.6. If the human subject research involves DOD-affiliated personnel, the key investigator must receive approval from the DOD-affiliated personnel's command or DOD Component to conduct the research. If the human subject research takes place on a DOD facility, the key investigator must also receive approval from the command or DOD Component responsible for the facility.

2.11.1.7. Only designated federal DOD HRPP personnel are authorized to make determinations regarding whether or not an activity is human subject research or is exempt human subject research.

2.11.1.8. DOD institutions collaborating in human subject research with non-DOD institutions may rely on the collaborating non-DOD institution's IRB if all of the following conditions are met:

2.11.1.8.1. The DOD institution determines the non-DOD institution has an appropriate federal assurance or that a federal assurance is not required.

2.11.1.8.2. The non-DOD institution's IRB is registered in accordance with Subpart E of Part 46 of Title 45, CFR.

2.11.1.8.3. The DOD institution reviews the protocol to ensure all applicable local and DOD requirements are addressed in the protocol.

2.11.1.8.4. The DOD institution and the non-DOD institution (including if the non-DOD institution uses an independent IRB) enter into an IAIR specifying that the non-DOD IRB will apply the DOD requirements specified in this issuance.

2.11.1.8.5. If the research constitutes classified human subject research, the component human research protection program management plan, on behalf of the senior designated official, approves the agreement to rely on the non-DOD institution's IRB.

2.11.1.9. DOD institutions conducting human subject research in collaboration with non-DOD institutions with or without DOD support must comply with all requirements in this issuance pertaining to DOD-conducted research.

2.11.2. DOD Component Administrative Review and Oversight.

2.11.2.1. The DOD Component must conduct an administrative review (also known as a component-level administrative review (component-level administrative review)) of all non-exempt human subject research when any of the following conditions occur:

2.11.2.1.1. Human subject research is conducted in a foreign country, unless conducted by a DOD overseas institution, or only involves DOD-affiliated personnel who are U.S. citizens.

2.11.2.1.2. The research requires a waiver of informed consent pursuant to Subsection (b) of Section 980 of Title 10, U.S.C.

2.11.2.1.3. The research is fetal research, as described in Sections 289g–289g-2 of Title 42, U.S.C.

2.11.2.1.4. large-scale genomic data is collected from DOD-affiliated personnel.

2.11.2.1.5. The research constitutes classified human subject research as defined by this issuance.

2.11.2.1.6. Research is required to be approved by the DOD Office for Human Research Protections

2.11.2.2. DOD administrative and DOD Component security reviews must be conducted before research involving large-scale genomic data collected from DOD-affiliated personnel may begin.

2.11.2.3. The DOD Component may, with DOD Office for Human Research Protections approval, delegate Component review and oversight of Sections 3.5.b.(1)(a) - (f) to a DOD institution.

2.12. DOD-SUPPORTED RESEARCH

2.12.1. DOD Component Approval and Oversight.

2.12.1.1. The DOD Component must conduct a component-level administrative review of all non-exempt human subject research when any of the following conditions occur:

2.12.1.1.1. Research is conducted in a foreign country, unless it is conducted by a DOD overseas institution, or involves subjects who are DOD-affiliated personnel that are U.S. citizens.

2.12.1.1.2. The research requires a waiver of informed consent pursuant to Paragraph (b) of Section 980 of Title 10, U.S.C.

2.12.1.1.3. The research is fetal research as described in Sections 289g–289g-2 of Title 42, U.S.C.

2.12.1.1.4. large-scale genomic data is collected from DOD-affiliated personnel.

2.12.1.1.5. The research constitutes classified human subject research as defined by this issuance.

2.12.1.1.6. Research is required to be approved by the DOD Office for Human Research Protections.

2.12.1.2. DOD administrative and DOD Component security reviews must be conducted before research involving large-scale genomic data collected from DOD-affiliated personnel may begin.

2.12.1.3. The DOD Component may, with DOD Office for Human Research Protections approval, delegate DOD Component review and oversight of Sections 3.5.b.(1)(a) - (f) to a DOD institution.

2.12.2. DOD institutions planning to support human subject research must comply with the requirements in this paragraph, as applicable.

2.12.2.1. Support for activities including research involving human subjects must consider Defense Federal Acquisition Regulation Supplement Defense Federal Acquisition Regulation Supplement) Section 207.172 requirements as part of the acquisition planning process. All Federal Acquisition Regulation (Federal Acquisition Regulation)–based contracts for DOD-supported research that include or may include human subject research must contain the Defense Federal Acquisition Regulation Supplement clause 252.235-7004 in its entirety in accordance with Defense Federal Acquisition Regulation Supplement Section 235.072(e).

2.12.2.1.1. All solicitations, including broad agency announcements, for DOD-supported research that include or may include human subject research must contain the Defense Federal Acquisition Regulation Supplement clause 252.235-7004, if the solicitation is for a Federal Acquisition Regulation-based contract or substantially similar language if the solicitation is for a non-Federal Acquisition Regulation-based agreement; and language referencing the National Policy Requirements Concerning Live Organisms Terms and Conditions, Section A.1., Human Subjects, at 81 Federal Register 78380, Appendix C to Part 1122. In addition to identifying DOD and non-DOD institutions' responsibilities, the role of the human research protection official is described in these two directives.

2.12.2.1.2. Agreements other than contracts that include or may include human subject research, but are not subject to Defense Federal Acquisition Regulation Supplement clause

252.235-7004 (e.g., grants, assistance agreements), must state the non-DOD institution's responsibilities. Including language referencing the National Policy Requirements Concerning Live Organisms Terms satisfies the requirements of this paragraph.

2.12.2.2. Contracts and other agreements (e.g., grants, assistance agreements) must:

2.12.2.2.1. Restrict the performance of prospective DOD-supported human subject research before the human research protection official's concurrence is provided.

2.12.2.2.2. Be awarded before an official human research protection official review is provided, although a non-binding human research protection official review may be conducted before award.

2.12.2.3. DOD institutions must appoint or designate human research protection official(s) to confirm that DOD-supported human subject research complies with this issuance.

2.12.2.4. Defense Federal Acquisition Regulation Supplement clause 252.235-7004 is not required to be included in a DOD agreement with another federal agency for DOD-supported human subject research. However, these agreements must include language requiring the federal agency to apply Sections 3.8, 3.9, 3.10, 3.11 and 3.13 of this issuance, and Section 1520a of Title 50, U.S.C.

2.12.2.5. When a DOD IRB serves as the reviewing IRB pursuant to Part 219 of Title 32, CFR, the DOD IRB approval will constitute the human research protection official review; an additional human research protection official review is not required.

2.12.2.6. The non-DOD institution:

2.12.2.6.1. For non-exempt human subject research, must submit to the human research protection official:

2.12.2.6.1.1. Documentation that the DOD-supported human subject research has been reviewed and approved by an IRB, including scientific merit, amendments, and additional reviews.

2.12.2.6.1.2. Documentation of key investigators' human research protection training.

2.12.2.6.1.3. IRB-approved protocol documents.

2.12.2.6.1.4. Current FWA and IRB registration numbers.

2.12.2.6.2. For DOD-supported research that is exempt or does not involve human subjects, must submit institutional documentation of the determination that the research is either not human subject research, exempt human subject research, or limited IRB review to the human research protection official, to include all protocol documents.

2.12.2.6.3. Must comply with all reporting requirements that may otherwise be applicable, in addition to the human research protection official reporting and submission requirements in this section.

2.12.2.6.4. Must promptly notify the human research protection official of the following:

2.12.2.6.4.1. IRB-approved changes to human subject research that involve changes to key investigators or institutions; decreased benefit or increased risk to subjects in greater than minimal risk research as defined in Part 219 of Title 32; addition of vulnerable populations, or DOD-affiliated personnel as subjects.

2.12.2.6.4.2. Transfer of human subject research oversight to a different IRB.

2.12.2.6.4.3. Notification by any federal body, State agency, official governing body of a Native American or Alaskan native tribe, other entity, or foreign government that the non-DOD institution's DOD-supported human subject research is under investigation.

2.12.2.6.4.4. Any problems involving risks to subjects or others, suspension or termination of IRB approval, or any serious or continuing noncompliance pertaining to DOD-supported human subject research.

2.12.2.6.4.5. The results of the IRB's continuing review, if required.

2.12.2.6.4.6. Change in status when a previously enrolled human subject becomes pregnant, or when the researcher learns that a previously enrolled human subject is pregnant, and the protocol was not reviewed and approved by the IRB in accordance with Subpart B, Subpart 46 of Title 45, CFR.

2.12.2.6.4.7. Change in status when a previously enrolled human subject becomes a prisoner, and the protocol was not reviewed and approved by the IRB in accordance with Subpart C, Subpart 46 of Title 45, CFR.

2.12.2.6.4.8. A DOD-supported study's closure.

2.12.2.6.4.9. Must make records that document compliance or noncompliance with this issuance accessible for inspection and copying, as determined by DOD HRPP personnel, by authorized DOD representatives.

2.12.2.6.4.10. Will recognize that failure to comply with applicable requirements may result in the DOD: Wholly or partially terminating or suspending the award; Temporarily withholding payment under the award pending correction of the deficiency; Disallowing all or part of the cost of the activity or action that is not in compliance; and/or Contacting publishers of articles that reference the noncompliant human subject research.

2.12.2.6.4.11. Will recognize that DOD-supported research should comply with the whole of this issuance when applicable.

2.13. DOD-ASSISTED RESEARCH.

2.13.1. Each component human research protection program management plan must establish policy to oversee the DOD Component's execution of DOD-assisted research or delegate the responsibility to create such policy to the DOD Component's institutions. To the extent consistent with this issuance, a DOD Component may waive some procedures applicable to DOD-supported human subject research when the DOD support is limited to assistance (as defined in this issuance).

2.14. SELECTION OF HUMAN SUBJECTS AND EVALUATING RISK.

2.14.1. The selection of human subjects in DOD-conducted or DOD-supported human subject research must comply with Section 252 of the National Defense Authorization Act for Fiscal Year 1994 (Public Law 103-160), with respect to gender, minority participation, and membership in the Armed Services. The authority to waive the requirements of this statute may be delegated in the component human research protection program management plan.

2.14.2. The definition of minimal risk in Part 219 of Title 32, CFR, does not include the inherent occupational risks that certain subjects face in their everyday life, such as those:

2.14.2.1. Encountered by Service members, law enforcement, or first responders while on duty.

2.14.2.2. Resulting from or associated with high-risk behaviors or pursuits.

2.14.2.3. Experienced by individuals whose medical conditions involve frequent tests or constant pain.

2.15. ADDITIONAL PROTECTIONS FOR HUMAN SUBJECTS.

2.15.1. Provide additional safeguards for subjects who are likely to be vulnerable to coercion or undue influence in accordance with Subparts B, C, and D of Part 46 of Title 45, CFR, and this issuance.

2.15.1.1. The additional safeguards set forth in Sections 3.9(b)-(f) must be provided in DOD-conducted and DOD-supported human subject research.

2.15.1.2. The DOD Office for Human Research Protections may delegate the authority for implementation of Subparts B, C, and D of Part 46 of Title 45, CFR, to the DOD Components' senior designated officials within their component human research protection program management plan.

2.15.2. Research involving pregnant women, fetuses, or neonates as human subjects must comply with Subpart B of Part 46, Title 45, CFR, unless modified by this issuance.

2.15.2.1. For purposes of applying this section, the phrase "biomedical knowledge" in Subpart B of Part 46, Title 45, CFR, is replaced with "generalizable knowledge."

2.15.2.2. The applicability of Subpart B of Part 46, Title 45, CFR, is limited to research involving pregnant women as human subjects involved in human subject research that is greater than minimal risk, and includes interventions, as defined in Part 219 of Title 32, CFR, or invasive procedures involving:

2.15.2.2.1. The woman or the fetus; or

2.15.2.2.2. Fetuses or neonates as human subjects.

2.15.2.3. Human subject research using fetal tissue must comply with Sections 289g–289g-2 of Title 42, U.S.C.

2.15.2.4. For human subject 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. DOD institutions must demonstrate to the senior designated official that the IRB has fulfilled its duties in accordance with Subpart B of Part 46, Title 45, CFR. Before human subject research activities may begin, the senior designated official must receive explicit written approval from the DOD Office for Human Research Protections.

2.15.3. Human subject research involving prisoners as human subjects must comply with Subpart C of Part 46 of Title 45, CFR, unless modified by this issuance.

2.15.3.1. In addition to the categories of permissible human subject research involving prisoners identified in Subpart C of Part 46 of Title 45, CFR, two additional categories are permissible:

2.15.3.1.1. Epidemiological research that meets the waiver criteria in accordance with Pages 36929-36931 of Volume 68, Federal Register, may be approved in accordance with the applicable requirements of Subpart C of Part 46 of Title 45, CFR, this issuance, and other applicable requirements.

2.15.3.1.2. Human subject research that would otherwise meet exemption criteria may be conducted but must first be approved by an IRB and must meet the requirements in Subpart C of Part 46 of Title 45, CFR, this issuance, and other applicable requirements.

2.15.3.2. DOD institutions conducting research involving prisoners must demonstrate to the senior designated official that the IRB has fulfilled its duties in accordance with Subpart C of Part 46 of Title 45, CFR.

2.15.3.3. When a previously enrolled human subject becomes a prisoner, and the protocol has not been reviewed and approved by the IRB in accordance with Subpart C of Part 46 of Title 45, CFR, the key investigator must promptly notify the IRB. For DOD-conducted research, the human protections director must notify the component human research protection program management plan. For DOD-supported research, the non-DOD institution must notify the human research protection official and other federal agencies, if required.

2.15.4. Human subject research involving children as human subjects must comply with Subpart D of Part 46 of Title 45, CFR. DOD institutions must demonstrate to the senior designated official that the IRB has fulfilled its duties in accordance with Part 407 of Subpart D of Part 46 of Title 45, CFR, and Section 50.54 of Title 21, CFR.

2.15.5. Research involving a detainee or a prisoner of war as a human subject is prohibited.

2.15.5.1. The prohibition in this paragraph does not apply to activities covered by investigational new drug or investigational device provisions of Title 21, CFR, when the purpose is for diagnosis or treatment of a medical condition in a patient.

2.15.5.2. Such treatment may be offered to detainees or prisoners of war with their informed consent when the medical products are subject to Title 21, CFR, and only when the same product may be available to DOD-affiliated personnel consistent with established medical practices.

2.15.6. DOD-affiliated Personnel as subjects in DOD-conducted or –supported human subject research.

2.15.6.1. If the human subject research involves DOD-affiliated personnel as subjects and if the human subject research includes any risks to their

fitness for duty (e.g. health, availability to perform job, data breach), the informed consent document (INFORMED CONSENT DOCUMENT) must inform DOD-affiliated personnel about these risks and that they should seek command or Component guidance before participating.

2.15.6.2. If the human subject research involves DOD-affiliated personnel, the key investigator must receive command or Component approval to execute the research.

2.15.6.3. Military and civilian supervisors, officers, and others in the chain of command are prohibited from influencing their subordinates to participate in human subject research.

2.15.6.4. Military and civilian supervisors, officers, and others in the chain of command must not be present at any human subject research participant recruitment sessions or during the human subject research consent process for DOD-affiliated personnel. Excluded supervisors or those in the chain of command may participate in separate human subject research recruitment sessions, if applicable.

2.15.6.5. Service members and all Reserve Component and National Guard members in a federal duty status are considered for purposes of this issuance, to be adults. If a Service member, Reserve Component or National Guard member in federal duty status, student at a Service Academy, or trainee is under 18 years of age, the IRB must carefully consider the human subject research recruitment process and the necessity of including such member as a human subject.

2.15.6.6. In order to approve research involving DOD-affiliated personnel as human subjects, the IRB or human research protection official must determine whether the following requirements have been satisfied:

2.15.6.6.1. The consent documentation must include, if applicable, potential risks for the revocation of clearance, credentials, or other privileged access or duty.

2.15.6.6.2. For research involving recruitment of DOD-affiliated personnel in human subject research determined greater than minimal risk, as defined by Part 219 of Title 32, CFR, and when human subject research recruitment occurs in a group setting, the IRB must appoint an ombudsperson. The ombudsperson:

2.15.6.6.2.1. Must not have a conflict of interest with the research or be a part of the research team.

2.15.6.6.2.2. Must be present during the human subject research recruitment, monitoring that the recruitment and informed consent explain that participation is voluntary and that the information provided about the research is consistent with the IRB-approved script and materials, including digitally provided materials.

2.15.6.6.2.3. Should be available to address DOD-affiliated personnel's concerns about participation.

2.15.6.7. Compensation to DOD-affiliated personnel for participation in research while on duty is prohibited in accordance with Title 5, U.S.C., with particular reference to Subparts G and H, with some exceptions for purposes consistent with Section 30 of Title 24, U.S.C.

2.16. Research involving large-scale genomic data collected on DOD-affliated personnel.

2.16.1. DOD-conducted or DOD-supported research involving large-scale genomic data collected on DOD-affiliated personnel, or for which research the DOD provides assistance, is subject to additional requirements in this issuance.

2.16.2. The disclosure of DOD-affiliated personnel's genomic data may pose a risk to national security; accordingly, such research requires administrative, technical, and physical safeguards commensurate with risk, including the secondary use or sharing of de-identified data or specimens.

2.16.3. All research involving large-scale genomic data collected from DOD-affiliated personnel will apply an HHS Certificate of confidentiality pursuant to Title 42, U.S.C., and Public Law 114-255.

2.16.4. Research involving large-scale genomic data collected from DOD-affiliated personnel is subject to DOD Component security review to ensure the adequacy of the proposed administrative, technical, and physical safeguards, including the secondary use or sharing of de-identified data or specimens.

2.17. UNIQUE DOD LIMITATIONS ON WAIVER OF INFORMED CONSENT.

2.17.1. Sections 219.116(e) and (f) of Title 32, CFR, identify conditions where an IRB may waive informed consent for DOD-conducted and DOD-supported human subject research.

2.17.2. Section 980 of Title 10, U.S.C.:

2.17.2.1. Imposes limitations on waiving informed consent when DOD appropriated funds are used to finance the research.

2.17.2.2. Is applicable only to DOD-conducted and DOD-supported research when involving a human being as an experimental subject as defined in this issuance. Research involving a human being as an experimental subject, governed by Section 980 of Title 10, U.S.C., is a subset of research involving human subjects, regulated by Title 32, CFR.

2.17.2.3. Is not applicable to exempt human subject research.

2.17.3. For research involving a human being as an experimental subject to which Section 980 of Title 10, U.S.C., applies, informed consent must be obtained in advance from the experimental subject or the subject's legal representative (consistent with Part 219 of Title 32, CFR, if the subject cannot consent). If consent is obtained from the subject's legal representative, the intention of the key investigator must be for the research to be beneficial to the subject.

2.17.4. For research governed by Section 980 of Title 10, U.S.C., that involves no more than minimal risk, as defined by Part 219 of Title 32, CFR, an IRB may alter or waive other required elements of informed consent pursuant to Part 219 of Title 32, CFR, so long as it still preserves informed consent of the subject (i.e., the consent indicates the subject's participation in the research is completely voluntary and includes the requirement that the subject is informed of research risks).

2.17.5. The advance informed consent requirement pursuant to Section 980 of Title 10, U.S.C., may be waived by the DOD Office for Human Research Protections or its delegate, if the following conditions are met:

2.17.5.1. The research is to advance the development of a medical product necessary to the DOD.

2.17.5.2. The research may directly benefit the individual experimental subject.

2.17.5.3. The research is conducted in compliance with all other applicable laws and regulations.

2.18. 3.12. PROTECTING HUMAN SUBJECTS FROM MEDICAL EXPENSES IF INJURED

2.18.1. DOD-Supported Research Involving Human Subjects.

2.18.2. All non-exempt human subject research must meet the requirement in Section 219.116 of Title 32, CFR.

2.18.3. DOD-Conducted Research Involving Human Subjects.

2.18.4. All human subject research that is determined to be greater than minimal risk must meet the requirement of Section 219.116 of Title 32, CFR, to provide subjects with an explanation as to whether any compensation and any medical treatments are available for research–related injuries.

2.18.4.1. Explanations must include a statement that subjects may, for the duration of the study, be eligible for health care services for research-related injuries at a military treatment facility, in accordance with Part 108 of Title 32, CFR. This eligibility for health care services extends beyond subjects' participation in the study to such time after the study has ended, in accordance with Section 219.108 of Title 32, CFR.

2.18.4.2. CMPs and institutional HRPPs must document how institutions will care for subjects with research-related injuries, including injuries that are the direct result of activities performed by DOD-affiliated personnel in studies that are collaborative with a non-DOD institution.

2.18.4.3.) Subjects injured in DOD-conducted research may obtain care for such injuries at a DOD medical treatment facility on a space-available basis during the pendency of the research study in accordance with DOD instruction 6025.23.

2.19. CLASSIFIED human subject research.

2.19.1. Pursuant to Parts 22, 37, and 219 of Title 32, CFR, and Sections 2.101 and 252.235-7004 of Title 48, CFR, and Executive Order 13526 DOD-conducted or DOD-supported human subject research is considered classified human subject research when:

2.19.1.1. Classified information is required for IRB review and oversight of the research.

2.19.1.2. Classified information must be provided to human subjects, or their guardians, during the human subject research recruitment or informed consent process in order to achieve fully effective legal consent.

2.19.1.3. Classified information is provided to, or by, research subjects.

2.19.2. DOD-conducted or –supported human subject research is not considered classified human subject research:

2.19.2.1. If the human subject research is a part of a classified program, but the research itself is not classified; if the information required in the research protocol is not classified; if the information needed by the IRB is not classified; or if the information required by the human subject is not classified. For the purposes of the annual report for classified research, unclassified human subject research that falls into the criteria listed in this paragraph should be included in the report.

2.19.2.2. Human subject research that requires subjects to hold a clearance as a means of creating ease of entry or access to controlled spaces where the research will occur does not constitute classified human subject research unless one of the conditions described in Sections 3.13.b.(1) or (3) also exist.

2.19.2.3. If the research constitutes an authorized operational activity, then it is not human subject research.

2.19.3. The DOD Office for Human Research Protections is the final approval authority for all DOD-conducted or DOD-supported classified human subject research. The senior designated official prospectively conducting or supporting the human subject research must submit a package to the DOD Office for Human Research Protections for approval to conduct the classified human subject research.

2.19.4. No DOD agency within the Intelligence Community may sponsor, contract for, or conduct non-exempt human subject research except in accordance with Paragraph 2.10 of Executive Order 12333 and DOD 5240.1.

2.20. There are certain authorities that the DOD Components may consider using for sensitive research.

2.20.1. Confidential Information Protection and Statistical Efficiency Act for Non-Statistical Agencies.

2.20.2. Any DOD Component may use the authority pursuant to Sections 501-513 of the Confidential Information Protection and Statistical Efficiency Act of 2002 (CIPSEA) (Public Law 107-347) to assure that data or information acquired by the 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. Use of this authority is subject to the requirements of CIPSEA Sections 512 and 523-525 and of Volume 72, Federal Register.

2.20.3. A DOD institution conducting human subject research or non-DOD institution conducting human subject research with DOD support may request a Certificate of confidentiality pursuant to Section 241 of Title 42, U.S.C. All studies involving large-scale genomic data collected on DOD-affiliated personnel will apply an HHS Certificate of confidentiality.

2.20.3.1. A Certificate of confidentiality prohibits disclosing or providing, in any federal, State, or local civil, criminal, administrative, legislative, or other proceeding, or to any other person not connected with the research, the name of any individual or any such information, document, or biospecimen that contains identifiable information about the individual, created or compiled for purposes of research.

2.20.3.2. Exceptions to the Certificate of confidentiality must be listed in all informed consent documents, pursuant to this issuance and as stated in Section 241 of Title 42, U.S.C.

2.21. RECORD-KEEPING.

2.21.1. Part 219 of Title 32, CFR, requires all institutions engaged in DOD-conducted or DOD-supported human subject research to retain records for at least 3 years after the completion of the research, or longer if required by DOD Manual 6025.18, the Privacy Act, FDA regulations, or other applicable requirements.

2.21.2. For complete record-keeping guidance and instruction, DOD institutions must consult their records disposition schedules.

2.21.3. Records maintained by non-DOD institutions that document compliance or noncompliance with this issuance must be accessible for inspection and copying by authorized representatives of the DOD

2.22. NONCOMPLIANCE.

2.22.1. DOD institutions must promptly respond to allegations of noncompliance with this issuance.

2.22.2. For allegations involving a non-DOD institution, the non-DOD institution must conduct an investigation in accordance with the applicable support agreement, to be furnished to the supporting DOD organization via the human research protection official. The DOD institution supporting the human subject research must ensure in its agreements with the non-DOD institution that allegations are promptly and properly investigated. The DOD institution will then promptly report substantiated serious and/or continuing non-compliance findings to the component human research protection program management plan.

2.22.3. Substantiated allegations related to classified human subject research must be reported immediately to the DOD Office for Human Research Protections.

2.23. The Coordinating Committee for Human Research Protection Programs is composed of senior officials at the general officer/flag officer, Senior Executive Service, or equivalent level.

2.23.1. Each senior designated official must identify one regular and one alternate member to represent their component to the Coordinating Committee for Human Research Protection Programs, and must promptly notify the DOD Office for Human Research Protections if those designations change.

2.23.2. The Coordinating Committee for Human Research Protection Programs Chair is the Director, Human Systems Directorate, Office of the Under Secretary of Defense for Research and Engineering.

2.23.3. The Executive Secretariat to the Coordinating Committee for Human Research Protection Programs is composed of the component human research protection program management plan directors, or equivalent authorities from the DOD Component HRPP oversight bodies, and those deemed necessary to the Executive Secretariat's missions by the DOD Office for Human Research Protections Director.

2.23.3.1. The Executive Secretariat is referred to as the DOD Office for Human Research Protections Cabinet; its Chair is the Director, DOD Office for Human Research Protections.

2.23.3.2. The DOD Office for Human Research Protections Cabinet acts as a central advisory committee to the DOD, the Under Secretary of Defense for Research and Engineering, and the DOD Office for Human Research Protections on matters regarding human subject research, privacy issues in research, ethical, legal and social implications in research.

2.23.3.3. The DOD Office for Human Research Protections Cabinet may act as an ethics panel or body and designate subcommittees as needed.

3. REFERENCES

3.1. 10 USC 980
3.2. DOD Instruction 3216.02
3.3. DOD Instruction 3216.2
3.4. OPNAVINST 5300.8B
3.5. SECNAVINST 3900.39D

4. REVISION HISTORY

4.1. **Edition 004**: Extensive updates for revised DoD Instruction 3216.02
4.2. **Edition 003:** Move information about civilian researchers, add information about surveys across DOD components, change references to officers and non-commissions officers to superiors of service members, add reference to recruitment in a group setting.
4.3. **Edition 002**: Updates based on revised guidance

1. PURPOSE

1.1. This guidance outlines the additional obligations of investigators conducting research supported or conducted by DOE.

2. GUIDANCE

2.1. Requirements for human participant protections and their accompanying Contractor Requirements Documents (CRDs) apply to all research conducted at DOE institutions regardless of funding source, or by DOE employees/contractor personnel regardless of funding source or location conducted, and whether done domestically or in an international environment, and including Human Terrain Mapping research.

2.1.1. The IRB considers DOE workers (employees and contractors) to be vulnerable subjects.

2.1.2. The IRB must consider if additional protections are required for research involving employees and contractors.

2.2. No human participant research conducted with DOE funding at DOE institutions (Headquarters or sites/laboratories, regardless of funding source), or by DOE employees and contractor personnel (regardless of funding source or location conducted), and whether done domestically or in an international environment, including classified and proprietary research, shall be initiated without both a Federalwide Assurance and approval by the cognizant IRB in accordance with 10 CFR Part 745.103.

2.3. Within 48 hours (or immediately upon discovery, if private identifiable information is involved), report to the IRB:

2.3.1. Any significant adverse events, unanticipated problems, and complaints about the research, with a description of any corrective actions taken or to be taken.

2.3.2. Any <Suspension of IRB Approval> <Termination of IRB Approval>;

2.3.3. Any significant <Noncompliance> with HRPP procedures or other requirements, which shall be reported to the IRB for evaluation for further action with the appropriate DOE Human Subject Protection Program Manager

2.4. In accordance with the DOE “Checklist for IRBs to Use in Verifying that HS Research Protocols are In Compliance with DOE Requirements,” the protocol must comply with the DOE requirements for protecting personally identifiable information (PII). Specifically, the protocol must include a description of processes for:

2.4.1. Keeping private identifiable information confidential

2.4.2. Releasing private identifiable information only under a procedure approved by the responsible IRB(s) and DOE, where required

2.4.3. Using private identifiable information only for purposes of the DOE-approved research

2.4.4. Handling and marking documents containing private identifiable information as “containing private identifiable information” or “containing protected health information”

2.4.5. Establishing reasonable administrative, technical, and physical safeguards to prevent unauthorized use or disclosure of private identifiable information

2.4.6. Making no further use or disclosure of the private identifiable information except when approved by the responsible IRB and DOE, where applicable, and then only:

2.4.6.1. In an emergency affecting the health or safety of any individual

2.4.6.2. For use in another research project under these same conditions and with DOE written authorization

2.4.6.3. For disclosure to a person authorized by the DOE program office for the purpose of an audit related to the project or when required by law.

2.4.7. Protecting private identifiable information data stored on removable media using encryption products that are Federal Information Processing Standards (FIPS) 140-2 certified

2.4.8. Using FIPS 140-2 certified encryption that meet the current DOE password requirements cited in DOE Guide 205.3-1

2.4.9. Shipping removable media containing PII, as required, by express overnight service with signature and tracking capability, and shipping hard copy documents double wrapped via express overnight service

2.4.10. Encrypting data files containing PII that are being sent by e-mail with FIPS 140-2 certified encryption products

2.4.11. Sending passwords that are used to encrypt data files containing PII separately from the encrypted data file, i.e. separate e-mail, telephone call, separate letter

2.4.12. Using FIPS 140-2 certified encryption methods for websites established for the submission of information that includes PII

2.4.12.1. Using two-factor authentication for logon access control for remote access to systems and databases that contain PII.

2.4.12.2. In addition to other reporting requirements, reporting the loss or suspected loss of PII immediately (within 5 business days) upon discovery to: 1) the DOE Project Officer and 2) the applicable IRBs.

2.4.13. For research conducted at a DOE facility, the DOE Institutional Official is responsible for:

2.4.13.1. Ensuring the Central DOE Review Board and the Central DOE Institutional Review Board-Classified comply with applicable requirements.

2.4.13.2. Formally appointing the chair, vice-chair, and other IRB members

2.4.13.3. Approving classified research conducted with DOE funding at its sites/laboratories and by its employees and contractors after IRB approval and prior to initiation.

2.5. When conducting classified research:

2.5.1. Requirements for human participant protections for classified research apply to all research conducted or supported by the DOE, including contracts, and including Human Terrain Mapping research.

2.5.2. The following are prohibited:

2.5.2.1. Use of exemptions

2.5.2.2. Use of the expedited review procedure

2.5.2.3. Waiver of the consent process

2.5.2.4. Waiver of documentation of consent

2.5.3. The IRB must have a voting quorum of at least five members, which must include both a non-scientist and a non-affiliated member.

2.5.4. The non-affiliated member must be a non-governmental member with the appropriate security clearances. This individual cannot be a current federal employee or contractor.

2.5.5. Any IRB member can appeal a vote to approve research to the Institutional Official, Secretary of Energy, and Director of the Office of Science and Technology, in that order.

2.5.6. In accordance with the DOE “Checklist for IRBs to Use in Verifying that HS Research Protocols are In Compliance with DOE Requirements,” the protocol must comply with the DOE requirements for protecting personally identifiable information (PII).

2.5.7. The IRB will determine if participants need access to classified information to make a valid consent decision.

2.5.8. Consent documents must include additional DOE elements of disclosure:

2.5.8.1. The identity of the sponsoring agency, unless the sponsor requests that it not be done, because doing so could compromise intelligence sources or methods; the research involves no more than minimal risk to participants; and the IRB determines that by not disclosing the identity, the investigators will not adversely affect the participants.

2.5.8.2. When research is classified, consent documents must state the project is classified, and what it means for the purposes of the research project

2.6. For research conducted at a DOE facility, the DOE Institutional Official is responsible for:

2.6.1. Ensuring the Central DOE Review Board and the Central DOE Institutional Review Board-Classified comply with applicable requirements.

2.6.2. Formally appointing the chair, vice-chair, and other IRB members.

2.6.3. Approving classified research conducted with DOE funding at its sites/laboratories and by its employees and contractors after IRB approval and prior to initiation.

2.7. For research conducted at a DOE facility, the DOE Human Subjects Protection Program Manager is responsible for:

2.7.1. Developing procedures for the classified research program in consultation with the National Nuclear Safety Administration Human Subject Protection Program Manager.

2.7.2. Conducting biennial performance reviews of all IRBs that review classified research involving human participants to assess compliance, in consultation with the National Nuclear Security Administration HRPP manager.

2.7.3. Reviewing and approving local plans to correct noncompliance or mitigate adverse events and unanticipated problems involving risks to participants or others.

2.7.4. Reviewing and approving statements of work for classified Human Terrain Mapping projects submitted by DOE's non-National Nuclear Security Administration sites or projects.

2.7.5. Making recommendations to the Secretary after concurrence from the organizational Official, on a project by project basis, regarding exemptions from the requirements for classified research.

2.7.6. Concurring on human participant provisions for classified research in interagency agreements, in consultation with the National Nuclear Security Administration, as appropriate.

2.7.7. Maintaining an unclassified list of classified projects.

2.8. The organization periodically conducts self-assessments to ensure compliance with the HRPP procedures and other requirements.

3. REFERENCES

3.1. 10 CFR 745

3.2. DOE Order 443.1.B

3.3. Checklist for IRBs to Use in Verifying That HS Research Protocols Are in Compliance with DOE Requirements – http://www.cgirb.com/wp-content/uploads/2019/03/Checklist-IRBs-Use-Verify-HS -Research-Comply-with -DOE -Requirements.ppt

4. REVISION HISTORY

4.1. **Edition 005**: Add IRB considers DOE workers to be vulnerable subjects; add that corrections actions taken must be provided for certain reports; remove reference to NIST two-factor authentication; clarify unaffiliated member requirements.

4.2. **Edition 004**: Extensive updates based on current guidance and AAHRPP standards updates

4.3. **Edition 003**: Updates based on revised guidance

1. PURPOSE

1.1. This guidance outlines the additional obligations of investigators conducting research supported or conducted by DOJ.

2. GUIDANCE

2.1. National Institute of Justice (NIJ)-funded research

2.1.1. Investigators must have a privacy certificate approved by the NIJ human subjects protection officer.

2.1.2. Investigators and research staff must sign employee confidentiality statements, and investigators must maintain these statements.

2.1.3. Investigators must obtain written informed consent and disclose

2.1.3.1. The names of the funding agencies.

2.1.3.2. The extent to which confidentiality of records identifying the subject will be maintained.

2.1.3.3. Private, identifiable information will be kept confidential and will only be used for research and statistical purposes.

2.1.3.3.1. If, due to sample size or some unique feature, the identity of the individual cannot be maintained, the participants need to be explicitly notified. If the investigator intends to disclose any information, the participant needs to be explicitly informed what information would be disclosed, under what circumstances, and to whom. The participant must be informed of any risks that might result from this disclosure and must explicitly provide written consent prior to participating in the research.

2.2. Research conducted within the Bureau of Prisons

2.2.1. The Department of Justice does not consider implementation of Bureau of Prisons programmatic or operational initiatives made through pilot projects to be research.

2.2.2. Investigators must follow the requirements of 28 CFR 512.:

2.2.3. The research must not involve medical experimentation, cosmetic research, or pharmaceutical testing.

2.2.4. The research design must be compatible with both the operation of prison facilities and protection of human subjects.

2.2.5. The investigator must observe the rules of the institution or office in which the research is conducted.

2.2.6. The Bureau of Prisons Research Review Board must approve the research.

2.2.7. The research must have an adequate research design and contribute to the advancement of knowledge about corrections.

2.2.8. The selection of subjects within any one organization must be equitable.

2.2.9. Incentives may not be offered to help persuade inmate subjects to participate. Soft drinks and snacks to be consumed at the test setting may be offered.

2.2.10. Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research subjects who are both:

2.2.10.1. No longer in Bureau of Prisons custody

2.2.10.2. Participating in authorized research being conducted by Bureau of Prisons employees or contractors

2.2.11. Except as noted in the consent statement to the subject, the investigator 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.

2.2.12. Except for computerized data records maintained at an official Department of Justice 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.

2.2.13. If the investigator is conducting a study of special interest to the Office of Research and Evaluation (ORE) but the study is not a joint research involving ORE, the investigator may be asked to provide ORE 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 research.

2.2.14. Consent documents must disclose:

2.2.14.1. Identification of the principal investigator(s)
2.2.14.2. Objectives of the research project
2.2.14.3. Procedures to be followed in the conduct of research
2.2.14.4. Purpose of each procedure
2.2.14.5. Anticipated uses of the results of the research
2.2.14.6. A statement of benefits reasonably to be expected
2.2.14.7. A declaration concerning discomfort and risk, including a description of anticipated discomfort and risk
2.2.14.8. A statement that participation is completely voluntary and that the participant 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)
2.2.14.9. 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 an intent to commit future criminal conduct or harm himself/herself or someone else, or, if the subject is an inmate, indicates an intent to leave the facility without authorization.
2.2.14.10. A statement that participation in the research project will have no effect on the inmate participant's release date or parole eligibility
2.2.14.11. An offer to answer questions about the research project and
2.2.14.12. Appropriate additional information as needed to describe adequately the nature and risks of the research

2.2.15. If the investigator is an employee of the Bureau of Prisons:

2.2.15.1. The consent statement must include a declaration of the authority under which the research is conducted.
2.2.15.2. An investigator must obtain the subject's signature on the statement of informed consent, when:

2.2.15.2.1. The subject's activity requires something other than response to a questionnaire or interview; or
2.2.15.2.2. The Chief, ORE, determines the research project or data-collection instrument is of a sensitive nature.

2.2.16. If the investigator is NOT an employee of the Bureau of Prisons:

2.2.16.1. The investigator must sign a statement in which the investigator agrees to adhere to the requirements of 28 CFR 512.
2.2.16.2. The investigator 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.

2.2.16.3. Must present the statement of informed consent to the subject.

2.2.16.4. Must obtain the subject's signature on the statement of informed consent prior to initiating the research activity.

2.2.16.4.1. The investigator may not be required to obtain the signature if the investigator can demonstrate that the only link to the subject's identity is the signed statement of informed consent or that there is significantly more risk to the subject if the statement is signed.

2.2.16.5. The signed statement must be submitted to the chairperson of the appropriate local research review board.

2.2.17. Investigators must have academic preparation or experience in the area of study of the proposed research.

2.2.18. When submitting a research protocol, investigators must provide the following information:

2.2.18.1. A summary statement, which includes:

2.2.18.1.1. Names and current affiliations of the investigators.
2.2.18.1.2. Title of the study.
2.2.18.1.3. Purpose of the study.
2.2.18.1.4. Location of the study.
2.2.18.1.5. Methods to be employed.
2.2.18.1.6. Anticipated results.
2.2.18.1.7. Duration of the study.
2.2.18.1.8. Number of subjects (staff or inmates) required and amount of time required from each.
2.2.18.1.9. Indication of risk or discomfort involved as a result of participation.

2.2.18.2. A comprehensive statement, which includes:

2.2.18.2.1. Review of related literature.
2.2.18.2.2. Detailed description of the research method.
2.2.18.2.3. Significance of anticipated results and their contribution to the advancement of knowledge.
2.2.18.2.4. Specific resources required from the Bureau of Prisons.
2.2.18.2.5. Description of all possible risks, discomforts, and benefits to individual subjects or a class of subjects, and a discussion of the likelihood that the risks and discomforts will actually occur.

2.2.18.2.5.1. Description of steps taken to minimize any risks.

2.2.18.2.6. Description of physical or administrative procedures to be followed to:

2.2.18.2.6.1. Ensure the security of any individually identifiable data that are being collected for the study.
2.2.18.2.6.2. Destroy research records or remove individual identifiers from those records when the research has been completed.

2.2.18.2.7. Description of any anticipated effects of the research study on organizational programs and operations.
2.2.18.2.8. Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules.

2.2.18.2.9. A statement regarding assurances and certification required by federal regulations, if applicable.

2.2.19. Investigators must assume responsibility for actions of any person engaged to participate in the research as an associate, assistant, or subcontractor to the investigator.

2.2.20. At least once a year, investigators must provide the Chief, Office of Research and Evaluation, with a report on the progress of the research.

2.2.21. At least 12 working days before any report of findings is to be released, investigators must distribute one copy of the report with an abstract in the report of findings to each of the following:

2.2.21.1. The chairperson of the Bureau Research Review Board
2.2.21.2. The regional director
2.2.21.3. The warden of each institution that provided data or assistance

2.2.22. In any publication of results, investigators must acknowledge the Bureau's participation in the research.

2.2.23. Investigators expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.

2.2.24. Prior to submitting for publication the results of research conducted under this subpart, investigators must provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.

3. REFERENCES

3.1. 28 CFR §22,
3.2. 28 CFR §512

4. REVISION HISTORY

4.1. **Edition 002.1**: eliminate empty line item 2.2.16.6 present in error
4.2. **Edition 002**: Clarify applicable to investigators conducting research supported or conducted by DOJ; updated to match latest regulations, add elements of consent, add sections for investigators employed by Bureau of Prisons and not employed by Bureau of Prisons
4.3. **Edition 00.1**: Update logo and footer

1. PURPOSE

1.1. This guidance outlines the additional obligations of investigators conducting research supported or conducted by ED.

2. GUIDANCE

2.1. The Family Educational Rights and Privacy Act (FERPA) applies when investigators obtain student records or personal education information from an education program as defined as any program principally engaged in the provision of education, including, but not limited to, early childhood education, elementary and secondary education, postsecondary education, special education, job training, career and technical education, and adult education. FERPA requirements include:

2.1.1. An educational agency or institution may disclose personally identifiable information from an education record of a student without consent if the disclosure is part of an agreement between organizations or subjects conducting studies for, or on behalf of, educational agencies or institutions to:

2.1.1.1. Develop, validate, or administer predictive tests
2.1.1.2. Administer student aid programs
2.1.1.3. Improve instruction

2.1.2. A school district or postsecondary institution that uses this exception is required to enter into a written agreement with the organization conducting the research that specifies:

2.1.2.1. The determination of the exception
2.1.2.2. The purpose, scope, and duration of the study
2.1.2.3. The information to be disclosed
2.1.2.4. That information from education records may only be used to meet the purposes of the study stated in the written agreement and must contain the current requirements in Department of Education regulations on redisclosure and destruction of information
2.1.2.5. That the study will be conducted in a manner that does not permit personal identification of parents and students by anyone other than representatives of the Organization with legitimate interests
2.1.2.6. That the Organization is required to destroy or return all personally identifiable information when no longer needed for the purposes of the study
2.1.2.7. The time period during which the Organization must either destroy or return the information

2.1.3. Education records may be released without consent under FERPA if all personally identifiable information has been removed including:

2.1.3.1. Student's name and other direct personal identifiers, such as the student's social security number or student number
2.1.3.2. Indirect identifiers, such as the name of the student's parent or other family members; the student's or family's address, and personal characteristics or other information that would make the student's identity easily traceable; and date and place of birth and mother's maiden name
2.1.3.3. Biometric records, including one or more measurable biological or behavioral characteristics that can be used for automated recognition of an individual, including fingerprints, retina and iris patterns, voiceprints, DNA sequence, facial characteristics, and handwriting.
2.1.3.4. Other information that, alone or in combination, is linked or linkable to a specific student that would allow a reasonable person in the school

community, who does not have personal knowledge of the relevant circumstances, to identify the student with reasonable certainty.

2.2. For certain types of research directly funded by ED the Protection of Pupil Rights Amendment (PPRA) applies.

2.2.1. PPRA prohibits students from being required, as part of any research project, to submit without prior consent to surveys, psychiatric examination, testing, or treatment, or psychological examination, testing, or treatment, in which the primary purpose is to reveal information concerning one or more of the following:

2.2.1.1. Political affiliations or beliefs of the student or the student's parent
2.2.1.2. Mental or psychological problems of the student or the student's family
2.2.1.3. Sex behavior or attitudes
2.2.1.4. Illegal, anti-social, self-incriminating, or demeaning behavior
2.2.1.5. Critical appraisals of other individuals with whom respondents have close family relationships
2.2.1.6. Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers
2.2.1.7. Religious practices, affiliations, or beliefs of the student or student's parent
2.2.1.8. Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program

2.2.2. For certain types of research projects not directly funded by ED and conducted in a school that receives funding from ED: Policies and procedures include a process to verify compliance with ED regulations that schools are required to develop and adopt policies in conjunction with parents regarding the following:

2.2.2.1. The right of a parent of a student to inspect, upon the request of the parent, a survey created by a third party before the survey is administered or distributed by a school to a student

2.2.2.1.1. Any applicable procedures for granting a request by a parent for reasonable access to such survey within a reasonable period of time after the request is received

2.2.2.2. Arrangements to protect student privacy that are provided by the agency in the event of the administration or distribution of a survey to a student containing one or more of the following items (including the right of a parent of a student to inspect, upon the request of the parent, any survey containing one or more of such items):

2.2.2.2.1. Political affiliations or beliefs of the student or the student's parent
2.2.2.2.2. Mental or psychological problems of the student or the student's family
2.2.2.2.3. Sex behavior or attitudes
2.2.2.2.4. Illegal, anti-social, self-incriminating, or demeaning behavior
2.2.2.2.5. Critical appraisals of other individuals with whom respondents have close family relationships
2.2.2.2.6. Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers
2.2.2.2.7. Religious practices, affiliations, or beliefs of the student or the student's parent
2.2.2.2.8. Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program)

2.2.2.3. The right of a parent of a student to inspect, upon the request of the parent, any instructional material used as part of the educational curriculum for the student

2.2.2.4. Any applicable procedures for granting a request by a parent for reasonable access to instructional material received

2.2.2.5. The administration of physical examinations or screenings that the school or agency may administer to a student

2.2.2.6. The collection, disclosure, or use of personal information collected from students for the purpose of marketing or for selling that information (or otherwise providing that information to others for that purpose), including arrangements to protect student privacy that are provided by the agency in the event of such collection, disclosure, or use.

2.2.2.7. The right of a parent of a student to inspect, upon the request of the parent, any instrument used in the collection of personal information before the instrument is administered or distributed to a student

2.2.2.8. Any applicable procedures for granting a request by a parent for reasonable access to such instrument within a reasonable period of time after the request is received

2.3. Access to instructional material used in a research or experimentation program:

2.3.1. All instructional material, including teachers' manuals, films, tapes, or other supplementary instructional material, which will be used in connection with any research or experimentation program or project must be available for inspection by the parents or guardians of the children engaged in such research.

2.4. Definitions:

2.4.1. “Prior consent” means prior written consent of the parent or student, if the student is a student who has reached 18 years of age or is attending an institution of postsecondary education.

2.4.2. “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.

2.4.3. “Children” are persons not above age 21 enrolled in research not above the elementary or secondary education level, who have not reached the age of majority as determined under state law.

2.4.4. "Psychiatric or psychological examination or test" means a method of obtaining information, including a group activity, that is not directly related to academic instruction and that is designed to elicit information about attitudes, habits, traits, opinions, beliefs or feelings (34 CFR §98.4)

2.4.5. "Psychiatric or psychological treatment" means an activity involving the planned, systematic use of methods or techniques that are not directly related to academic instruction and that is designed to affect behavioral, emotional, or attitudinal characteristics of an individual or group (34 CFR §98.4)

3. REFERENCES

3.1. 34 CFR §98
3.2. 34 CFR §99
3.3. 34 CFR §356

4. REVISION HISTORY

4.1. **Edition 003:** Remove references to emancipated minor, replace with new info
4.2. **Edition 002:** Remove reference to NIDRR, clarify that this SOP applies to research conducted or supported by ED, add to definition of children “not above age 21”
4.3. **Edition 001.1:** Update logo and footer

INVESTIGATOR GUIDANCE: Additional EPA Obligations

Document No.:	Edition No.:	Effective Date:	Page:
HRP-814	002	18 Dec 2019	Page 1 of 1

1. PURPOSE

1.1. This guidance outlines the additional obligations of investigators conducting research supported or conducted by EPA or whose results are intended to be submitted to EPA.

2. GUIDANCE

2.1. EPA regulates research that is conducted or supported by EPA.
2.2. EPA regulates research whose results are intended to be submitted to EPA, regardless of whether the research is conducted or supported by EPA or any federal agency.
2.3. “Research involving intentional exposure of a human subject” means a study of a substance in which the exposure to the substance experienced by a human subject participating in the study would not have occurred but for the human subject's participation in the study.
2.4. “Observational research” means any human research that is not research involving intentional exposure of a human subject.
2.5. Research involving the intentional exposure of pregnant women, nursing women, or children to any substance is prohibited.
2.6. Observational research involving children must meet the criteria in category (1) or (2) of “CHECKLIST: Research Involving Children (HRP-310)”
2.7. Observational research involving pregnant women must meet the criteria in “CHECKLIST: Pregnant Women (HRP-305).”
2.8. Research approved by the IRB must be submitted to the EPA human subjects research review official for final review and approval before the research can begin.

3. REFERENCES

3.1. 40 CFR §26
3.2. EPA Order 1000.17 Change A1

4. REVISION HISTORY

4.1. **Edition 002:** expand purpose to include “supported or conducted by EPA or whose results are intended to be submitted to EPA”
4.2. **Edition 001.1:** Update logo and footer

1. PURPOSE

1.1. This guidance outlines the additional obligations of investigators conducting FDA research.

2. GUIDANCE

2.1. For all FDA-regulated research:

2.1.1. When a subject withdraws from a study:

2.1.1.1. The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed.

2.1.1.1.1. The consent document cannot give the subject the option of having data removed.

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

2.1.1.3. 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, you 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.

2.1.1.4. If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, you must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent.

2.1.1.4.1. You may review study data related to the participant collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.

2.1.2. The Responsible Party for a clinical trial must register the trial and submit results information.

2.1.2.1. A principal investigator of a clinical trial is the Responsible Party if the clinical trial is investigator initiated or if so designated by a sponsor, grantee, contractor, or awardee.

2.1.2.2. Registration is required for the following trials:

2.1.2.2.1. Controlled clinical investigations, other than phase 1 clinical investigations, of drugs or biological products

2.1.2.2.2. Controlled trials with health outcomes of devices, other than small feasibility studies

2.1.2.2.3. Pediatric post-market surveillance required by FDA

2.2. Requirements for studies conducted under an IND

2.2.1. You, or any person acting on your behalf, cannot 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.

2.2.1.1. 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.

2.2.2. You may not commercially distribute or test market an investigational new drug.

2.2.3. Ensure that the 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 your care; and for the control of drugs under investigation.

2.2.4. Obtain the informed consent of each human subject to whom the drug is administered, unless:

2.2.4.1. Waived by the IRB for planned emergency research.

2.2.4.2. Where the requirements in “WORKSHEET: Emergency Use - Drugs and Biologics (HRP-451)” are met

2.2.5. Maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects.

2.2.5.1. If the investigation is terminated, suspended, discontinued, or completed, return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies as directed by the sponsor.

2.2.6. 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.

2.2.6.1. 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 chart(s), and the nurses’ notes.

2.2.6.2. The case history for each individual must document that informed consent was obtained prior to participation in the study.

2.2.7. Retain research records for the greater of:

2.2.7.1. Three years after completion of the research

2.2.7.2. For drug studies conducted under an IND, two 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 two years after the investigation is discontinued and FDA is notified.

2.2.7.3. For device studies conducted under an IDE or abbreviated IDE, two years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol.

2.2.7.4. The retention period requested by the sponsor.

2.2.8. Furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.

2.2.9. Immediately report to the sponsor any serious adverse event, whether or not considered drug related, including those listed in the protocol or investigator brochure.

2.2.9.1. The report must include an assessment of whether there is a reasonable possibility that the drug caused the event.

2.2.9.2. Study endpoints that are serious adverse events (e.g., all-cause mortality) must be reported in accordance with the protocol unless there is evidence suggesting a causal relationship between the drug and the event (e.g., death from anaphylaxis). In that case, immediately report the event to the sponsor.

2.2.9.3. Record non-serious adverse events and report them to the sponsor according to the timetable for reporting specified in the protocol.

2.2.10. Provide the sponsor with an adequate report shortly after completion of your participation in the investigation.

2.2.11. Provide the sponsor with sufficient accurate financial information to allow an applicant to submit complete and accurate certification or disclosure statements as required under part 54 of this chapter.

2.2.11.1. Promptly update this information if any relevant changes occur during the course of the investigation and for one year following the completion of the study.

2.2.12. Assure that an IRB that complies with the requirements set forth in FDA regulations will be responsible for the initial and continuing review and approval of the proposed clinical study.

2.2.12.1. Promptly report to the IRB all changes in the research activity and all <Unanticipated Problems Involving Risk to Subjects or Others>.

2.2.12.2. Make no changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

2.2.13. 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 of your records or reports.

2.2.13.1. You are 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.

2.2.14. If the investigational drug is subject to the Controlled Substances Act, 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.

2.3. Requirements for studies conducted under an abbreviated IDE

2.3.1. You, or any person acting for or on behalf of you may not:

2.3.1.1. Promote or test market the investigational device, until after FDA has approved the device for commercial distribution.

2.3.1.2. Commercialize the investigational device by charging the subjects or investigators for a device a price larger than that necessary to recover costs of manufacture, research, development, and handling.

2.3.1.3. Unduly prolong the investigation.

2.3.1.4. Represent that the investigational device is safe or effective for the purposes for which it is being investigated.

2.3.2. If the study is investigator-initiated:

2.3.2.1. Label the device as follows:

2.3.2.1.1. The device or its immediate package must bear a label with the following information: the name and place of business of the manufacturer, packer, or distributor (in accordance with §801.1), the quantity of contents, if appropriate, and the following statement: “CAUTION-Investigational device. Limited by Federal (or United States) law to investigational use.” The label or other labeling shall describe all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings, and precautions.

2.3.2.1.2. The device must not bear any statement that is false or misleading in any particular and shall not represent that the device is safe or effective for the purposes for which it is being investigated.

2.3.2.2. Comply with the requirements of 21 CFR §812.46 with respect to monitoring investigations.

2.3.2.3. Maintain the records required under 21 CFR §812.140(b) (4) and (5) and makes the reports required under 21 CFR §812.150(b) (1) through (3) and (5) through (10).

2.3.2.4. Ensure that participating investigators maintain the records required by 21 CFR §812.140(a)(3)(i) and make the reports required under 21 CFR §812.150(a) (1), (2), (5), and (7).

2.3.3. Ensure that the 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 your care, and for the control of devices under investigation.

2.3.3.1. Ensure that informed consent is obtained in accordance with FDA regulations.

2.3.4. You may determine whether potential subjects would be interested in participating in an investigation, but do not request the written informed consent of any subject to participate, and do not allow any subject to participate before obtaining IRB and FDA approval.

2.3.5. Conduct the investigation in accordance with the signed agreement with the sponsor, the investigational plan, this part and other applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.

2.3.6. Permit the investigational device to be used only with subjects under your supervision.

2.3.6.1. Do not supply an investigational device to any person not authorized under this part to receive it.

2.3.7. Disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements required by FDA regulations.

2.3.7.1. Promptly update this information if any relevant changes occur during the course of the investigation and for one year following completion of the study.

2.3.8. Upon completion or termination of a clinical investigation or your part of an investigation, or at the sponsor's request, return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.

2.3.9. Maintain the following accurate, complete, and current records relating to the your participation in an investigation:

2.3.9.1. Records of each subject's case history and exposure to the device. Case histories include:

2.3.9.1.1. 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 chart(s), and the nurses' notes

2.3.9.1.2. Documents evidencing informed consent and, for any use of a device without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent. The case history for each individual must document that informed consent was obtained prior to participation in the study

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

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

2.3.10. Permit authorized FDA employees, at reasonable times and in a reasonable manner:

2.3.10.1. 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).

2.3.10.2. To inspect and copy all records relating to an investigation.

2.3.10.3. 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 you to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

2.3.11. Prepare and submit the following complete, accurate, and timely reports:

2.3.11.1. 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 10 working days after you first learn of the effect.

2.3.11.2. Report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of your part of an investigation.

2.3.11.3. If you use a device without obtaining informed consent, report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.

2.3.11.4. Upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

2.4. Expanded Access

2.4.1. FDA has an expanded access program, which allows the use of investigational new drugs and approved drugs where availability is limited by a risk evaluation and mitigation strategy (REMS) when the primary purpose is to diagnose, monitor, or treat a patient's disease or condition. The aim of expanded access is to facilitate the availability of such drugs to patients with serious diseases or conditions when there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the patient's disease or condition.

2.4.2. In all cases of expanded access, investigators are responsible for reporting adverse drug events to the sponsor, ensuring that the informed consent requirements of part 50 of this chapter are met, ensuring that IRB review of the expanded access use is obtained in a manner consistent with the requirements of part 56 of this chapter, and maintaining accurate case histories and drug disposition records and retaining records in a manner consistent with the requirements of §312.62. Depending on the type of expanded access, other investigator responsibilities under subpart D may also apply.

2.5. Requirements for studies conducted under an IDE

2.5.1. You, or any person acting for or on behalf of you may not:

2.5.1.1. Promote or test market the investigational device, until after FDA has approved the device for commercial distribution.

2.5.1.2. Commercialize the investigational device by charging the subjects or investigators for a device a price larger than that necessary to recover costs of manufacture, research, development, and handling.

2.5.1.3. Unduly prolong the investigation.

2.5.1.4. Represent that the investigational device is safe or effective for the purposes for which it is being investigated.

2.5.2. Ensure that the 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 your care, and for the control of devices under investigation.

2.5.2.1. Ensure that informed consent is obtained in accordance with FDA regulations.

2.5.3. You may determine whether potential subjects would be interested in participating in an investigation, but do not request the written informed consent of any subject to participate, and do not allow any subject to participate before obtaining IRB and FDA approval.

2.5.4. Conduct the investigation in accordance with the signed agreement with the sponsor, the investigational plan, this part and other applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.

2.5.5. Permit the investigational device to be used only with subjects under your supervision.

2.5.5.1. Do not supply an investigational device to any person not authorized under this part to receive it.

2.5.6. Disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements required by FDA regulations.

2.5.6.1. Promptly update this information if any relevant changes occur during the course of the investigation and for one year following completion of the study.

2.5.7. Upon completion or termination of a clinical investigation or your part of an investigation, or at the sponsor's request, return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.

2.5.8. Maintain the following accurate, complete, and current records relating to the your participation in an investigation:

2.5.8.1. All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.

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

2.5.8.2.1. The type and quantity of the device, the dates of its receipt, and the batch number or code mark

2.5.8.2.2. The names of all persons who received, used, or disposed of each device

2.5.8.2.3. Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of

2.5.8.3. Records of each subject's case history and exposure to the device. Case histories include:

2.5.8.3.1. 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 chart(s), and the nurses' notes.

2.5.8.3.2. Documents evidencing informed consent and, for any use of a device without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent. The case history for each individual must document that informed consent was obtained prior to participation in the study.

2.5.8.3.3. 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.

2.5.8.3.4. A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.

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

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

2.5.9. Permit authorized FDA employees, at reasonable times and in a reasonable manner:

2.5.9.1. 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).

2.5.9.2. To inspect and copy all records relating to an investigation.

2.5.9.3. 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 you to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

2.5.10. Prepare and submit the following complete, accurate, and timely reports:

2.5.10.1. 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 10 working days after you first learn of the effect.

2.5.10.2. Report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of your part of an investigation.

2.5.10.3. 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.

2.5.10.4. 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.

2.5.10.4.1. Give such notice as soon as possible, but in no event later than 5 working days after the emergency occurred.

2.5.10.4.2. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan.

2.5.10.4.3. If these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, prior approval of FDA and the IRB are required.

2.5.10.5. If you use a device without obtaining informed consent, report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.

2.5.10.6. Within 3 months after termination or completion of the investigation or your part of the investigation, submit a final report to the sponsor and the reviewing IRB.

2.5.10.7. Upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

3. REFERENCES

3.1. 21 CFR §312.60, §312.61, §312.62, §312.64, §312.66, §312.68, §312.69, §312.300, §312.305, §812.40, §812.42, §812.43, §812.45, §812.46

4. REVISION HISTORY

4.1. **Edition 001.2:** Triennial review - no changes

4.2. **Edition 001.1:** Update logo and footer

1. PURPOSE

1.1. This guidance outlines the additional obligations of investigators conducting research subject to ICH-GCP.

2. GUIDANCE

2.1. Investigator's Qualifications and Agreements

2.1.1. The investigator(s) 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 requirement(s), 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 authority(ies).

2.1.2. The investigator should be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.

2.1.3. The investigator should be aware of, and should comply with, GCP and the applicable regulatory requirements.

2.1.4. The investigator/institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authority(ies).

2.1.5. The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.

2.2. Adequate Resources

2.2.1. 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.

2.2.2. The investigator should have sufficient time to properly conduct and complete the trial within the agreed trial period.

2.2.3. 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.

2.2.4. The investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s), and their trial-related duties and functions.

2.2.5. The investigator is responsible for supervising any individual or party to whom the investigator delegates trial-related duties and functions conducted at the trial site.

2.2.6. If the investigator/institution retains the services of any individual or party to perform trial-related duties and functions, the investigator/institution should ensure this individual or party is qualified to perform those trial-related duties and functions and should implement procedures to ensure the integrity of the trial-related duties and functions performed and any data generated.

2.3. Medical Care of Trial Subjects

2.3.1. A qualified physician (or dentist, when appropriate), who is an investigator or a subinvestigator for the trial, should be responsible for all trial-related medical (or dental) decisions.

2.3.2. 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 illness(es) of which the investigator becomes aware.

2.3.3. 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.

2.3.4. Although a subject is not obliged to give his/her reason(s) for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reason(s), while fully respecting the subject's rights.

2.4. Communication with IRB

2.4.1. Before initiating a trial, the investigator/institution should have written and dated approval 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.

2.4.2. 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.

2.4.3. During the trial the investigator/institution should provide to the IRB all documents subject to review.

2.5. Compliance with Protocol

2.5.1. The investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authority(ies) and which was given approval by the IRB. The investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.

2.5.2. 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 of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g., change in monitor(s), change of telephone number(s)).

2.5.3. The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol.

2.5.4. The investigator may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard(s) to trial subjects without prior IRB approval. As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendment(s) should be submitted: a) to the IRB for review and approval, b) to the sponsor for agreement and, if required, c) to the regulatory authority(ies).

2.6. Investigational Product(s)

2.6.1. Responsibility for investigational product(s) accountability at the trial site(s) rests with the investigator/institution.

2.6.2. Where allowed/required, the investigator/institution may/should assign some or all of the investigator's/institution's duties for investigational product(s) accountability at the trial site(s) to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator/institution.

2.6.3. 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(s). These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product(s) 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(s) received from the sponsor.

2.6.4. The investigational product(s) should be stored as specified by the sponsor and in accordance with applicable regulatory requirement(s).

2.6.5. The investigator should ensure that the investigational product(s) are used only in accordance with the approved protocol.

2.6.6. The investigator, or a person designated by the investigator/institution, should explain the correct use of the investigational product(s) to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.

2.7. Randomization Procedures and Unblinding

2.7.1. 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(s).

2.8. Informed Consent of Trial Subjects

2.8.1. In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirement(s), 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 of the written informed consent form and any other written information to be provided to subjects.

2.8.2. 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.

2.8.3. Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial.

2.8.4. 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.

2.8.5. 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 by the IRB.

2.8.6. 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.

2.8.7. 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.

2.8.8. 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.

2.8.9. 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.

2.8.10. 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:

2.8.10.1. That the trial involves research
2.8.10.2. The purpose of the trial
2.8.10.3. The trial treatment(s) and the probability for random assignment to each treatment
2.8.10.4. The trial procedures to be followed, including all invasive procedures
2.8.10.5. The subject's responsibilities
2.8.10.6. Those aspects of the trial that are experimental
2.8.10.7. The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant
2.8.10.8. The reasonably expected benefits.

2.8.10.8.1. When there is no intended clinical benefit to the subject, the subject should be made aware of this

2.8.10.9. The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks
2.8.10.10. The compensation and/or treatment available to the subject in the event of trial-related injury
2.8.10.11. The anticipated prorated payment, if any, to the subject for participating in the trial
2.8.10.12. The anticipated expenses, if any, to the subject for participating in the trial
2.8.10.13. 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
2.8.10.14. That the monitor(s), the auditor(s), the IRB, and the regulatory authority(ies) 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

2.8.10.15. 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

2.8.10.16. If the results of the trial are published, the subject's identity will remain confidential 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

2.8.10.17. The person(s) 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

2.8.10.18. The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated

2.8.10.19. The expected duration of the subject's participation in the trial

2.8.10.20. The approximate number of subjects involved in the trial

2.8.11. 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 amendments to the written information provided to subjects.

2.8.12. 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.

2.8.12.1. Therapeutic trials (i.e. a trial in which there is 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.

2.8.13. 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 can not 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 of the IRB is expressly sought on the inclusion of such subjects, and the written approval 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.

2.8.14. 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, enrollment of the subject should require measures described in the protocol and/or elsewhere, with documented approval 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.

2.9. Records and Reports

2.9.1. The investigator/institution should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail).

2.9.2. 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.

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

2.9.4. 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 investigators' 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.

2.9.5. 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 requirement(s). The investigator/institution should take measures to prevent accidental or premature destruction of these documents.

2.9.6. Essential documents should be retained until at least 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 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.

2.9.7. The financial aspects of the trial should be documented in an agreement between the sponsor and the investigator/institution.

2.9.8. Upon request of the monitor, auditor, IRB, or regulatory authority, the investigator/institution should make available for direct access all requested trial-related records.

2.10. Progress Reports

2.10.1. The investigator should submit written summaries of the trial status to the IRB annually, or more frequently, if requested by the IRB.

2.10.2. 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.

2.11. Safety Reporting

2.11.1. All serious adverse events (SAEs) should be reported immediately to the 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 should also comply with the applicable

regulatory requirement(s) related to the reporting of unexpected serious adverse drug reactions to the regulatory authority(ies) and the IRB.

2.11.2. 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.

2.11.3. 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).

2.12. Premature Termination or Suspension of a Trial

2.12.1. 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 requirement(s), should inform the regulatory authority(ies). In addition:

2.12.2. 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.

2.12.3. 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.

2.12.4. If the IRB terminates or suspends its approval 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.

2.13. Final Report(s) by Investigator

2.13.1. 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 authority(ies) with any reports required.

2.14. Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP).

3. REFERENCES

3.1. ICH Topic E6 (R2) Guideline for Good Clinical Practice, (EMA/CHMP/ICH/135/1995), Step 4 Version, 9 November 2016.

4. REVISION HISTORY

4.1. **Edition 003:** Updates due to ICH Topic E6 (R2) Guideline for Good Clinical Practice, (EMA/CHMP/ICH/135/1995), Step 4 Version, 9 November 2016

4.2. **Edition 002.1:** Update logo and footer

1. PURPOSE

1.1. This guidance outlines the additional obligations of investigators conducting a <Clinical Trial> subject to ISO 14155.

2. GUIDANCE

2.1. General

2.1.1. The role of the principal investigator is to implement and manage the day-to-day conduct of the clinical investigation as well as ensure data integrity and the rights, safety and well-being of the subjects involved in the clinical investigation.

2.1.2. If the sponsor contracts an institution to conduct the clinical investigation, the institution shall appoint an appropriately qualified person to be the principal investigator.

2.2. Qualification of the principal investigator: The principal investigator shall

2.2.1. Be qualified by education, training and experience to assume responsibility for the proper conduct of the clinical investigation in accordance with this International Standard; evidence of such qualifications of the principal investigator and key members of the investigation site team shall be provided to the sponsor through up-to-date CVs or other relevant documentation.

2.2.2. Be experienced in the field of application and trained in the use of the investigational device under consideration.

2.2.3. Disclose potential conflicts of interest, including financial, that interfere with the conduct of the clinical investigation or interpretation of results.

2.2.4. Be knowledgeable with the method of obtaining informed consent.

2.3. Qualification of investigation site: The principal investigator shall be able to demonstrate that the proposed investigation site

2.3.1. Has the required number of eligible subjects needed within the agreed recruitment period.

2.3.2. Has one or more qualified investigators, a qualified investigation site team and adequate facilities for the foreseen duration of the clinical investigation.

2.4. Communication with the IRB: The principal investigator shall

2.4.1. Provide the sponsor with copies of any clinical-investigation-related communications between the principal investigator and the IRB.

2.4.2. Comply with the requirements to communicate with the IRB.

2.4.3. Obtain the written and dated approval/favourable opinion of the IRB for the clinical investigation before recruiting subjects and implementing all subsequent amendments, if required.

2.4.4. Perform safety reporting as specified below.

2.4.5. Promptly report any deviations from the clinical investigational plan that affect the rights, safety or well-being of the subject or the scientific integrity of the clinical investigation, including those which occur under emergency circumstances, if required by the IRB, clinical investigational plan or national regulations.

2.4.6. In particular circumstances, the communication with the IRB can be performed by the sponsor, partly or in full, in which case the sponsor shall keep the principal investigator informed.

2.5. Informed consent process: The principal investigator shall

2.5.1. Comply with the requirements specified by the IRB to obtain informed consent.

2.5.2. Ensure compliance with the applicable regulatory requirements and ethical principles for the process of obtaining informed consent.

2.5.3. Ensure and document appropriate training if an authorized designee is appointed to conduct the informed consent process.

2.6. Compliance with the clinical investigational plan: The principal investigator shall

2.6.1. Indicate his/her acceptance of the clinical investigational plan in writing.
2.6.2. Conduct the clinical investigation in compliance with the clinical investigational plan.
2.6.3. Create and maintain source documents throughout the clinical investigation and make them available as requested during monitoring visits or audits.
2.6.4. Ensure that the investigational device is used solely by authorized users as specified in 6.2, and in accordance with the clinical investigational plan and instructions for use.
2.6.5. Propose to the sponsor any appropriate modification(s) of the clinical investigational plan or investigational device or of the use of the investigational device.
2.6.6. Refrain from implementing any modifications to the clinical investigational plan without agreement from the sponsor, IRB and regulatory authorities, if required.
2.6.7. Document and explain any deviation from the approved clinical investigational plan that occurred during the course of the clinical investigation.
2.6.8. Ensure that an adequate investigation site team and facilities exist and are maintained and documented during the clinical investigation.
2.6.9. Ensure that maintenance and calibration of the equipment relevant for the assessment of the clinical investigation is appropriately performed and documented, where applicable.
2.6.10. Ensure the accuracy, completeness, legibility and timeliness of the data reported to the sponsor in the case report forms and in all required reports.
2.6.11. Maintain the device accountability records.
2.6.12. Allow and support the sponsor to perform monitoring and auditing activities.
2.6.13. Be accessible to the monitor and respond to questions during monitoring visits.
2.6.14. Allow and support regulatory authorities and the IRB when performing auditing activities.
2.6.15. Ensure that all clinical-investigation-related records are retained as required.
2.6.16.
2.6.17. Sign the clinical investigation report.

2.7. Medical care of subjects: The principal investigator shall

2.7.1. Provide adequate medical care to a subject during and after a subject's participation in a clinical investigation in the case of adverse events, as described in the informed consent.
2.7.2. Inform the subject of the nature and possible cause of any adverse events experienced.
2.7.3. Provide the subject with the necessary instructions on proper use, handling, storage and return of the investigational device, when it is used or operated by the subject.
2.7.4. Inform the subject of any new significant findings occurring during the clinical investigation, including the need for additional medical care that may be required.
2.7.5. Provide the subject with well-defined procedures for possible emergency situations related to the clinical investigation, and make the necessary arrangements for emergency treatment, including decoding procedures for blinded/masked clinical investigations, as needed.
2.7.6. Ensure that clinical records are clearly marked to indicate that the subject is enrolled in a particular clinical investigation.
2.7.7. If appropriate, subjects enrolled in the clinical investigation shall be provided with some means of showing their participation in the clinical investigation, together

with identification and compliance information for concomitant treatment measures (contact address and telephone numbers shall be provided).

2.7.8. Inform, with the subject's approval or when required by national regulations, the subject's personal physician about the subject's participation in the clinical investigation.

2.7.9. Make all reasonable efforts to ascertain the reason(s) for a subject's premature withdrawal from the clinical investigation while fully respecting the subject's rights.

2.8. Safety reporting: The principal investigator shall

2.8.1. Record every adverse event and observed device deficiency, together with an assessment.

2.8.2. Report to the sponsor, without unjustified delay, all serious adverse events and device deficiencies that could have led to a serious adverse device effect; this information shall be promptly followed by detailed

2.8.3. Written reports, as specified in the clinical investigational plan.

2.8.4. Report to the IRB serious adverse events and device deficiencies that could have led to a serious adverse device effect, if required by the national regulations or clinical investigational plan or by the IRB.

2.8.5. Report to regulatory authorities serious adverse events and device deficiencies that could have led to a serious adverse device effect, as required by the national regulations.

2.8.6. \supply the sponsor, upon sponsor's request, with any additional information related to the safety reporting of a particular event.

3. REFERENCES

3.1. ISO 14155 Clinical investigation of medical devices for human subjects — Good clinical practice

4. REVISION HISTORY

4.1. **Edition 001.1:** Triennial review - no changes

4.2. **Edition 001:** New SOP

1. PURPOSE

1.1. This guidance outlines the additional obligations of investigators conducting research supported or conducted by HHS.

2. GUIDANCE

2.1. Research is automatically covered by a certificate of confidentiality whenever the study is funded in whole or in part by the NIH and involves identifiable, sensitive information.

2.1.1. "Identifiable sensitive information" means information about an individual that is gathered or used during biomedical, behavioral, clinical, or other research, where the following may occur:

2.1.1.1. An individual is identified; or

2.1.1.2. For which there is at least a very small risk, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

2.1.2. Examples of research automatically covered by a certificate of confidentiality include:

2.1.2.1. Biomedical, behavioral, clinical or other research, including exempt research, except where the information obtained is recorded in such a manner that human subjects cannot be identified, or the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects.

2.1.2.2. The collection or use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual.

2.1.2.3. The generation of individual level, human genomic data from biospecimens, or the use of such data, regardless of whether the data is recorded in a manner that human subjects can be identified, or the identity of the human subjects can readily be ascertained.

2.1.2.4. Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

2.1.3. Investigators may also apply for a certificate of confidentiality for non-federally funded research.

2.1.4. When research is covered by a certificate of confidentiality, investigators:

2.1.4.1. May not disclose or provide, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, the name of such individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for purposes of the research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or

2.1.4.2. May not disclose or provide to any other person not connected with the research the name of such an individual or any information, document or biospecimen that contains identifiable, sensitive

information about such an individual and that was created or compiled for the purposes of the research.

2.1.4.3. May disclose information only when:

2.1.4.3.1. Required by Federal, State, or local laws (e.g., as required by the Federal Food, Drug, and cosmetic Act, or state laws requiring the reporting of communicable diseases to the State and local health departments), excluding instances of disclosure in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding.

2.1.4.3.2. Necessary for the medical treatment of the individual to whom the information, document, or biospecimen pertains and made with the consent of such individual.

2.1.4.3.3. Made with the consent of the individual to whom the information, document, or biospecimen pertains; or

2.1.4.3.4. Made for the purpose of other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects in research.

2.1.5. When research is covered by a certificate of confidentiality, investigators must inform subjects (for example, in the consent document) of the protections and limitations of certificates of confidentiality.

2.1.5.1. This requirement also applies to existing studies active on after December 13, 2016. For existing studies, investigators must notify subjects that the research is now covered by a certificate of confidentiality. However, because a certificate of confidentiality reduces risks, the IRB does not need to require the research to obtain consent again based in this information and can simply notify subjects of this change.

2.1.6. investigators conducting NIH-supported research covered by a certificate of confidentiality must ensure that if identifiable sensitive information is provided to other investigators or organizations, regardless of whether the research is federally funded, the other investigator or organization must comply with applicable requirements when the research is covered by a certificate of confidentiality.

2.2.

3. REFERENCES

3.1. 10 USC 980
3.2. DOD Instruction 3216.02
3.3. DOD Instruction 3216.2
3.4. OPNAVINST 5300.8B
3.5. SECNAVINST 3900.39D