1.14 Research Subject to Department of Defense Regulatory Requirements

1.0 Purpose

The purpose of this policy and procedure is to specify the Organization’s requirements for the review, approval, conduct and oversight of human subject research funded by or involving the U.S. Department of Defense (DoD) and the U.S. Department of the Navy (DoN).

2.0 Policy

- 2.1. It is the policy of the Organization that it will comply fully with all approval requirements of DoD and DoN when its IRBs review, approve and provide oversight of human subjects research funded by or otherwise contractually subject to DoD or DoN regulations and requirements or uses a DoD/DoN property, facility or asset.
- 2.2. It is the policy of the Organization that the research specified in Section 2.1 above will comply with the following codes, regulations, and guidance:
  - 2.2.1. The Belmont Report
  - 2.2.2. 32 CFR 219, Department of Defense Regulations, “Protection of Human Subjects” (DoD adoption of the “Common Rule”)
  - 2.2.3. Title 45 Code of Federal Regulations Part 46, (45 CFR 46) Department of Health and Human Services Regulations, “Protection of Human Subjects,” Subparts B, C, and D as made applicable by DoD Instruction (DoDI) 3216.02, 15 April 2020.
  - 2.2.4. Title 21 Code of Federal Regulations 50, 56, 312, and 812, Food and Drug Administration (FDA) Regulations
  - 2.2.5. DoDI 3216.02, “Protection of Human Subjects and Adherence to Ethical Standards in DoD-Conducted and -Supported Research” April 15, 2020, Change 1,

June 29, 2022.
    - 2.2.6. Title 10 United States Code Section 980 (10 USC 980), “Limitation on Use of Humans as Experimental Subjects”
    - 2.2.7. DoDD 3210.7, “Research Integrity and Misconduct”
    - 2.2.8. DoDD 6200.2, “Use of Investigational New Drugs in Force Health Protection”
    - 2.2.9. DoDI 1100.13, “DoD Surveys”, March 31, 2017.
    - 2.2.10. When conducting research supported by the Department of the Navy
        - 2.2.10.1. SECNAVINST 3900.39E of 29 May 2018
        - 2.2.10.2. OPNAVINST 5300.8C of 24 April 2008
- 2.3. It is the policy of the Organization that research specified in Section 2.1 will comply with the following requirements, as applicable:
    - 2.3.1. Education and Training Requirements In addition to investigator and research staff training requirements as described in HRPP policy 1.23 (HRPP Training Requirements and Opportunities for Research Personnel), it is the Principal Investigator’s responsibility to ensure that research staff has completed all appropriate educational requirements as mandated by DoD policy. (per DoDI 3216.02, 15 April 2020, or later; http://www.onr.navy.mil/About-ONR/compliance-protections/Research-Protections/Research-Protection-Training-References.aspx.)
    - 2.3.2. Additional Protections for Pregnant Women, Prisoners, and Children {Subparts B, C and D) of 45 CFR 46) DoDD 3216.02, section 3.9}. In addition to protections described in HRPP policies 4.2 (Research Involving Pregnant Women, Human Fetuses, and Neonates), 4.3 (Research Involving Prisoners), 4.4 (Research Involving Children), and other policies as applicable, the following additional protections apply:
        - 2.3.2.1. Regarding Research Involving Pregnant Women and Human Fetuses: Research involving pregnant women, fetuses, or neonates as human subjects must comply with 45 CFR 46 subpart B except as below:
          (1) For purposes of applying this section, the phrase “biomedical knowledge” is replaced with “generalizable knowledge.”
          (2) The applicability of 45 CFR 46 subpart B is limited to research involving pregnant women as human subjects involved in HSR that is greater than minimal risk, and includes interventions, as defined in 32 CFR 219, or invasive procedures involving:
          (a) The woman or the fetus; or
          (b) Fetuses or neonates as human subjects.
          (3) HSR using fetal tissue must comply with 42, U.S.C Chapter 6A, Subchapter III, Part H, 289g:
          • Research or experimentation may not be conducted, in the United States or in any other country, on a nonviable living human fetus ex utero or a living human fetus ex utero for whom viability has not been ascertained unless the research or experimentation:
          • May enhance the well-being or meet the health needs of the fetus or enhance the probability of its survival to viability; or
          • Will pose no added risk of suffering, injury, or death to the fetus and the purpose of the research or experimentation is the development of important biomedical knowledge which cannot be obtained by other means.
          • The risk standard must be the same for fetuses which are intended to be aborted and fetuses which are intended to be carried to term.

• 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, written approval from the DOHRP must be obtained through the HPRO prior to research starting.

- 2.3.2.2. Regarding Research Involving Prisoners Research involving prisoners as human subjects must comply with 45 CFR 46 subpart C except as below:
  - 2.3.2.2.1. In addition to the categories of permissible HSR involving prisoners identified in 45 CFR 46 subpart C two additional categories are permissible:
    (a) Epidemiological research that meets the waiver criteria in accordance with Federal Register 68: 36929-36931, may be approved in accordance with the applicable requirements of 45 CFR 46 subpart C, DoDI 3612.02 and other applicable requirements.
    (b) HSR that would otherwise meet exemption criteria may be conducted but must first be approved by an IRB and must meet the requirements in 45 CFR 46 subpart C, DoDI 3612.02, and other applicable requirements.
  - 2.3.2.2.2. When a previously enrolled human subject becomes a prisoner, and the protocol has not been reviewed and approved by the IRB in accordance with 45 CFR 46 subpart C, the PI must promptly notify the IRB and the Organization must notify the Human Research Protection Official (HRPO).
    - 2.3.2.2.2.1. All research interactions and interventions with the prisoner- subject (including obtaining identifiable private information) must cease until and unless:
      • The IRB Executive Chair or designee determines that it is in the best interest of the prisoner-participant to continue to participate in the research while a prisoner. In this case, the prisoner-participant may continue to participate until the convened IRB can review this request to approve a change in the research protocol and until the organizational official and DoD Component office review the IRB's approval to change the research protocol.; or
      • The convened IRB review and approves the protocol in accordance with 45 CFR 46 subpart C, DoDI 3612.02, and HRPP policy 4.3 (Research Involving Prisoners).
  - 2.3.2.2.3. Research may not involve detainees unless the research involves an investigational drug or device when the same product would be offered to members of the US military in the same location for the same medical condition.
  - 2.3.2.2.4. Research may not involve Prisoners of War.
  - 2.3.2.2.5. Research involving prisoners cannot be reviewed by the expedited review procedure.
- 2.3.2.3. Regarding Research Involving Children: Research involving children as human subjects must comply with 45 CFR 45 subpart D. The DoD considers all active duty service members and all reserve component members in a Federal duty status to be adults; and therefore not subject to the protections of 45 CFR 46 subpart D. However, in the state of Nebraska, the age of majority is 19 years. Therefore, the Organization restricts participation in DoD research to 19 years of age or older.

- 2.3.3. Additional Safeguards for Research Conducted with International Populations

  In addition to the requirements described in HRPP policy 1.5 (Requirements for Research Conducted at International Sites) the following apply:
  - 2.3.3.1. Research involving human subjects who are not U.S. citizens or DoD personnel, conducted outside the United States, and its territories and possessions requires permission of the host country.
  - 2.3.3.2. The institution shall confirm that all applicable national laws and requirements of the foreign country have been met. The IRB shall also consider the cultural sensitivities in the setting where the research will take place (SECNAVINST 3900.39E, section 3d).
  - 2.3.3.3. Approval by the appropriate DoD component is required prior to research starting when human subjects research is conducted in a foreign country, unless conducted by a DoD overseas institution, or only involves DoD-affiliated personnel who are US citizens.
- 2.3.4. Limitation of Waivers and Exceptions from Informed Consent
  - 2.3.4.1. 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 HSR.
  - 2.3.4.2. Section 980 of Title 10, U.S.C. (1) Imposes limitations on waiving informed consent when DoD appropriated funds are used to finance the research; (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; and (3) Is not applicable to exempt HSR.
  - 2.3.4.3. DoD component-level administrative review (CLAR) must be conducted when the research requires a waiver of informed consent pursuant to 10 USC 980, Subsection (b).
  - 2.3.4.4. 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.
  - 2.3.4.5. 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).
  - 2.3.4.6. The advance informed consent requirement pursuant to Section 980 of Title 10, U.S.C., may be waived by the DOHRP or its delegate, if the following conditions are met:
    (1) The research is to advance the development of a medical product necessary to the DoD;
    (2) The research may directly benefit the individual experimental subject; and

(3) The research is conducted in compliance with all other applicable laws and regulations.

- 2.3.5. Limitations on Compensation for U.S. Military Personnel
  - 2.3.5.1. Federal employees while on duty (including military personnel) may be compensated for blood draws for research for up to $50 for each blood draw. Compensation is not allowed for general research participation.
  - 2.3.5.2. Federal employees while off-duty (including military personnel) may be compensated for blood draws for research for up to $50 for each blood draw. Compensation is allowed for general research participation, as approved by the IRB; however, payment may not come directly from a federal source.
  - 2.3.5.3. Non-Federal personnel may be compensated for blood draws for research for up to $50 for each blood draw. Compensation is allowed for general research participation, as approved by the IRB; payment may come from any federal or non- federal source.
- 2.3.6. Requirements for Informed Consent Forms In addition to requirements described in HRPP policy 5.1 (Obtaining Informed Consent From Research Subjects) the following apply:
  - 2.3.6.1. If the research includes any risks to the fitness for duty for DoD personnel (e.g., health, availability to perform job, data breach), the informed consent document must inform DoD-affiliated personnel about these risks and that they should seek command or Component guidance before participating.
  - 2.3.6.2. The informed consent document must include, if applicable, potential risks for the revocation of clearance, credentials, or other privileged access or duty
  - 2.3.6.3. The informed consent document must include a statement that the DoD or a DoD organization is funding the study, and a statement that representatives of the DoD are authorized to review research records.
- 2.3.7. Provisions for Research with Human Subjects using Investigational Test Articles (Drugs, Device and Biologics): PIs may not be sponsors for INDs and IDEs.
- 2.3.8. Classified Research
  - 2.3.8.1. Classified research must receive prior approval from the DoD Office for Human Research Protections.
  - 2.3.8.2. Classified research will be conducted following the requirements of DoD Instruction 3216.02 section 3.13.
  - 2.3.8.3. Classified research is not eligible for review under expedited review procedures, or for a waiver of consent.
- 2.3.9. Undue Influence [DoDD 3216.02, para.4.4.4]
  - 2.3.9.1. Superiors are prohibited from influencing the decisions of their subordinates regarding participation as subjects in research involving human subjects and shall not be present at any human subject recruitment sessions or during the consent process.
  - 2.3.9.2. For research involving service members as human subjects that has been determined to be greater than minimal risk and when recruitment occurs in a group setting, the IRB shall appoint an ombudsman. The ombudsman shall not be associated in any way to the research and shall be present during the recruitment in order to monitor that the voluntary involvement or recruitment of the Service members is clearly and adequately stressed and that the information provided about the research is clear, adequate, and accurate.
  - 2.3.9.3. For research involving service members as human subjects, that has been determined to be NO greater than minimal risk and when recruitment

occurs in a group setting, and for research involving DoD civilians, the IRB shall determine when it is appropriate to appoint an ombudsman for the purposes described above. The decision to require the appointment of an ombudsman should be based in part on the human subject population, the consent process, and the recruitment strategy.

- 2.3.10. Requirements for Research Related Injury
  - 2.3.10.1. Consent for DoD-supported research that is greater than minimal risk must include information about available compensation or medical treatments if a research-related injury occurs.
  - 2.3.10.2. For research subject to Department of the Navy (DON) requirements, every project involving greater than minimal risk shall include an arrangement for emergency treatment and necessary follow-up of any research-related injury. The IRB will determine whether research involving minimal risk also might include a similar arrangement for research-related injury.
- 2.3.11. Requirements for Reporting
  - 2.3.11.1. When participating in DoD supported non-exempt human subject research, the organization must provide to the HRPO:
    (1) documentation that the DoD- supported HSR has been reviewed and approved by an IRB, including scientific merit, amendments, and additional reviews;
    (2) documentation of key investigators' human research protection training;
    (3) IRB-approved protocol documents; and
    (4) current FWA and IRB registration numbers.
  - 2.3.11.2. When participating in DoD supported exempt human subject research, the organization must submit institutional documentation of the determination that the research is exempt HSR to the HRPO, to include all protocol documents.
  - 2.3.11.3. When participating in DoD supported non-exempt human subject research the Organization must promptly (within 30 days) notify the HRPO of the following:
    - 2.3.11.3.1. IRB-approved changes to HSR that involve changes to key investigators or institutions; decreased benefit or increased risk to subjects in greater than minimal risk research as defined in 32 CFR 219; addition of vulnerable populations, or DoD-affiliated personnel as subjects.
    - 2.3.11.3.2. Transfer of HSR oversight to a different IRB.
    - 2.3.11.3.3. 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 HSR is under investigation.
    - 2.3.11.3.4. Any unanticipated problems involving risks to subjects or others, suspension or termination of IRB approval, or any serious or continuing noncompliance pertaining to DoD-supported HSR.
    - 2.3.11.3.5. The results of the IRB's continuing review, if required.
    - 2.3.11.3.6. 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 45 CFR 46 subpart B.
    - 2.3.11.3.7. 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 45 CFR 46 subpart C.
    - 2.3.11.3.8. A DoD-supported study's closure.
  - 2.3.11.4. When participating in DoD supported non-exempt human subject research the Organization must make records that document compliance or noncompliance with DoDI 3612.02 accessible for inspection and copying, as determined by DoD Human Research Protection Program personnel, by authorized DoD representatives.
  - 2.3.11.5. When participating in DoN supported non-exempt human subject research, the organization must inform the Department of the Navy (DON) HRPP Office (within 30 days of the incident) of any of the following:
    - 2.3.11.5.1. The initiation and results of investigations into allegations of noncompliance.
    - 2.3.11.5.2. Serious adverse events; or audits, investigations, or inspections of research.
    - 2.3.11.5.3. Audits, investigations, or inspections of the Organization HRPP conducted by outside entities.
    - 2.3.11.5.4. Significant communication between institutions conducting research and other federal departments and agencies regarding compliance and oversight.
    - 2.3.11.5.5. All restrictions, suspensions, or terminations of the Organization assurances.
  - 2.3.12. Requirements for a Medical Monitor: For DoD-supported research, prior to April 15, 2020, a named independent research monitor was required for greater than minimal risk research and was optional for minimal risk research. As of April 15, 2020, a research monitor is no longer required by the DoD for DoD-supported research, regardless of risk level.
- 2.3.13. Requirements for Survey Research:
  - 2.3.13.1. The Principal Investigator for any DoD-supported research involving surveys is responsible for arranging for the review of the survey by the appropriate DoD component. This review is in addition to review by the IRB. For DON funded survey research, a Privacy Act Statement must be displayed prominently on all Navy personnel surveys. The statement will identify the authority for survey administration (including OPNAV RCS), advise respondents of the purpose and routine uses of the survey, indicate that the survey is voluntary, explain the intended use(s) of the data, and describe measures used to safeguard confidentiality (OPNAVINST 5300.8C).
  - 2.3.13.2. Surveys performed on DoD personnel must be submitted, reviewed, and approved by the DoD Information Management Control Officer (IMCO) after the research protocol is reviewed and approved by the IRB. When a survey crosses DoD components, additional review is required. The Principal Investigator is responsible for this process and should work with the DoD component to obtain approval.
- 2.3.14. Requirements for DoD Oversight: The HRPP will support the oversight by the sponsoring DoD component, including communicating to the sponsoring DoD component about:
  - 2.3.14.1. information needed to assure that the approval of the initial submission is in compliance with all applicable requirements; and
  - 2.3.14.2. IRB-approved substantive changes, including a notification that the Principal Investigator is informed that the changes cannot be implemented prior to acceptance by the sponsoring DoD component; and

    - 2.3.14.3. the results of the continuing review; and
    - 2.3.14.4. other information reported as required by section 2.3.11 (Requirements for Reporting) above.
  - 2.3.15. Research involving Chemical or Biological Agents
    - 2.3.15.1. The organization does not permit research involving chemical or biological agents.
  - 2.3.16. Confidentiality of Research Data
    - 2.3.16.1. 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 (per DoDI 3216.02 June 29, 2022)
    - 2.3.16.2. All studies involving large scale genomic data collected on/from DoD-affiliated personnel will apply an DHHS Certificate of Confidentiality (per DoDI 3216.02 June 29, 2022).

3.0 Definitions

- 3.1. For DoD supported research, the following definitions apply (and supersede definitions in other HRPP policies) Research Involving a Human Being as an Experimental Subject - An activity, for research purposes, where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Research involving a human being as an experimental subject is a subset of research involving human subjects. This definition relates only to the application of Section 980 of Title 10, U.S.C.; it does not affect the application of Part 219 of Title 32, CFR.
  - 3.1.1. Minimal Risk - the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (32 CFR 219). This definition does not include does not include the inherent occupational risks that certain subjects face in their everyday life, such as those:
    (1) encountered by Service members, law enforcement, or first responders while on duty;
    (2) resulting from or associated with high-risk behaviors or pursuits;
    (3) experienced by individuals whose medical conditions involve frequent tests or constant pain (DoDI 3216.02 section 3.8b).
  - 3.1.2. DoD Components - refers collectively to the organizational entities within the DoD that are subject to the human subjects protections laid out in Department of Defense Instructions (DoDI) 3216.02. These entities include the Office of the Secretary of Defense (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.
    - 3.1.3. Support of a Study - funds or assistance that are provided by the DoD to non-DoD institutions for HSR through a grant, contract, or similar arrangement subject to the DFARS or other applicable DoD regulations, such as the DoD Grant and Agreement Regulations. Included in this definition is the DoD's provision of assistance to non-DoD institutions, whether or not through collaboration between DoD and non-DoD institutions, such as facilities, equipment, personnel (investigators or other personnel performing tasks identified in the research protocol), access to or information about DoD-affiliated personnel for recruitment, or data or specimens.
    - 3.1.4. Detainee - any individual captured by, or transferred to the custody or control of, DoD personnel pursuant to the law of war. This does not include persons being held solely for law enforcement purposes, except where the United States is the occupying power. Detainees who are U.S. citizens or U.S. resident aliens will continue to enjoy all applicable rights and privileges under U.S. law and DoD regulations (DoDD 2310.01E).
    - 3.1.5. DoD Personnel - Service members, Reserve Service members, National Guard members, DoD civilians, and DoD contractors. (DoDI 3216.02).
    - 3.1.6. Service Members - Individuals appointed, enlisted, or inducted for military service under the authority of the DoD. The Military Services are the Army; the Navy, including the Coast Guard under circumstances involving the declaration of war; the Air Force; the Marine Corps; and the Reserve Components. Members of the Reserve Components are included when in a duty status.
    - 3.1.7. Human Research Protection Official (HRPO) - A federal employee designated by a DoD Component or institution to conduct administrative review of DoD-supported research and whose review of DoD-supported research is intended to ensure compliance with DoD HSR requirements.

4.0 Procedures

- 4.1. When reviewing research subject to DoD regulatory requirements, IRB members will be provided with a copy of this policy (HRPP policy 1.14) along with the IRB application, consent form, protocol, and all other related documents.
- 4.2. The IRB will review the application and consult the Research Subject to Department of Defense Research Regulatory Requirements Checklist to ensure compliance with all applicable DoD requirements, DoN requirements, and requirements of this and all other HRPP policies.
- 4.3. As appropriate and required (per section 2.3.9 above) the IRB will appoint an ombudsman to protect the rights of service members.
- 4.4. The IRB Analyst responsible for the protocol will assure that the PI has:
    - 4.4.1. Notified appropriate DoD entities, as described above, and confirmed that the DoD component has conducted an administrative review as required by DoDI 3612.02 section 3.5b.

    - 4.4.2. Uploaded a copy of the DoD component approval and all applicable additional DoD approvals, including, but not limited to, those required for survey, waiver or international research in the RSS system. Research will not be released until the appropriate DoD approvals are on file.
- 4.5. The IRB Analyst responsible for the protocol will:
    - 4.5.1. Assure the Organization has a valid FWA as required by DoDI 3612.02 section 3.4a.
    - 4.5.2. Assure that the requirements of this policy are met.
    - 4.5.3. Assure that the informed consent form complies with provisions of section 2.3.6 (Requirements for Informed Consent Forms) above.
    - 4.5.4. Make reports to the DoD (or have the PI make reports to the DoD) as described above.

DOCUMENT HISTORY:

? Written: 4/13/2016 (Approved: 4/13/2016) - original author not recorded

? Revised: 3/3/2018 - revision not documented

? Revised: 6/4/2021 - Reorganized; extensive revisions based on revisions to DoDI 3216.02, 15 April 2020, SECNAVINST 3900.39E, 29 May 2018

? Revised: 8/7/2023 - added 2.3.15 and 2.3.16; revised 2.3.4 per DoDI 3216.02, April 15, 2020 Change 1, June 29, 2022 {Approved Rusty McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

? Revised 1/10/2024 - Revised section 2.3.2.1 to describe specific restrictions associated with 42 USC Chapter 6A, Subchapter III, Part H, 289g; revised section 2.3.3 to specify that approval by the appropriate DoD component is required prior to research starting when human subjects research is conducted in a foreign country; revised section 2.3.4 to specify that DoD component-level administrative review (CLAR) must be conducted when the research requires a waiver of informed consent pursuant to 10 USC 980, Subsection (b); revised section 2.3.13 to specify that surveys performed on DoD personnel must be submitted, reviewed, and approved by the DoD Information Management Control Officer (IMCO) after the research protocol is reviewed and approved by the IRB; revised section 4.4.2 to clarify that the IRB Analyst responsible for the protocol will assure that the PI has uploaded a copy of the DoD component approval and all applicable additional DoD approvals, and that research will not be released until the appropriate DoD approvals are on file; other minor wording changes for clarity. {Approved Rusty McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

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