POLICY

1. Purpose

Outline the additional federal regulatory requirements required under Department of Defense (DoD) Directive Instruction 3216.02 entitled "Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research."

2. Scope

This policy applies to any employee or agent of the University of Rochester conducting research involving a human being as an experimental subject funded by the DoD, recruiting individuals from the DoD or a DoD component (the Office of the Secretary of Defense, the Military Departments, Joint Chiefs of Staff, Combatant Commands, and all other organizational entities within the DoD), or recruiting DoD personnel through a contract, grant, cooperative agreement, or other arrangement.

3. Definitions

3.1. *Classified research involving human subjects* - Research involving human subjects where the protocol or other information required by the IRB for review and oversight, or required or provided by the research subjects, includes classified information.

3.2. *COHRP* – Component Office of Human Research Protections.

3.3. *Component-Level Administrative Review* (CLAR) - A review of a research protocol and supporting documents (e.g., safety review, scientific review, IRB minutes, reliance agreements) to ensure the institution engaged in the research involving human subjects has met the requirements of all applicable regulations and policies. This review is NOT an IRB review.

3.4. *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.

3.5. *DoD Personnel* - DoD civilian employees and members of the military services.

3.6. *DoD-affiliated Personnel* –Military Service members (e.g., Army, Navy, Marines, Air Force, National Guard, Coast Guard, the Reserve Components, which includes the Army and the Air National Guards of the US.), Reserve Service members, DoD civilian employees, and DoD contractors.

3.7. *DOHRP*- DoD Office for Human Research Protections.

3.8. *Human Research Protection Official (HRPO)*- A federal employee designated by a DoD component or institution to conduct administrative review of DoD-supported research in accordance with the requirements of the Defense Federal Acquisition Regulation Supplement (DFARS) or comparable requirement, and whose review of DoD-supported research is intended to ensure compliance with DoD regulations and policies.

3.9. *Large-Scale Genomic Data (LSGD)* - includes data derived from genome-wide association studies; single nucleotide polymorphisms arrays; genome sequencing, transcriptomic, metagenomic, epigenomic analyses; and gene expression data. Examples of research involving LSGD includes, but is not limited to, projects that involve generating the whole genome sequence data for more than one gene from more than 1,000 individuals or analyzing 100 or more genetic variants in more than 1,000 individuals.

3.10. *Ombudsperson*: A person who acts as an impartial and objective advocate for human subjects participating in research.

3.11. *Prisoner of War (POW)* - A detained person as defined in Articles 4 and 5 of the Geneva Convention Relative to the Treatment of Prisoners of War of August 12, 1949. In particular, one who, while engaged in combat under orders of his government, is captured by the armed forces of the enemy.

3.12. *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.

4. References

4.1. HHS 45 CFR 46; FDA 21 CFR 56;

4.2. United States Code, Title 10, Sections 139 and 980;
Department of Defense 32 CFR 219;
DoD Instruction 3216.02 "Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research"

4.3. Policy 504 IRB Reliance and Collaborative Research;
Policy 505 Scientific Review Standards;
Policy 601 Research Involving Children;
Policy 602 Research Involving Pregnant Women, Human Fetuses, and Neonates;
Policy 603 Research Involving Prisoners;
Policy 608: Research Involving Genetic Testing and Gene Transfer;

Policy 801 Reporting Research Events;
Policy 802 Non-compliance in Human Subjects Research;
609a Checklist for RSRB Review of Research Supported by the DoD
Guideline for Reporting Research Events;
Guideline for Institutional and Regulatory Reporting of Suspension, Termination, Non-Compliance and UPIRTSO;
Guideline for Conducting International Research;
University of Rochester Policy on Research Misconduct

5. Responsibilities

5.1. Investigators and research staff are responsible for compliance with DoD research ethics training requirements.

5.2. Investigators are responsible for ensuring compliance with DoD regulatory requirements when conducting research supported by DoD in addition to the University and OHSP policies and guidelines applicable to the conduct of human subject research.

5.2.1. When research involves U.S. military personnel, Investigators must follow federal regulations that limit dual compensation:

- DoD-affiliated personnel who participate in research while on duty are prohibited from receiving subject payment.
- U.S. military personnel may be compensated for research if the participant is involved in the research *when not on duty*, provided payment does not conflict with prohibitions about dual compensation or other prohibitions in federal law.
- Federal employees while on duty and non-federal persons may be compensated for blood draws for research up to $50 for each blood draw.
- Non-federal persons may be compensated for research participation other than blood draws in a reasonable amount as approved by the Reviewing IRB according to local prevailing rates and the nature of the research.

5.3. Investigators are responsible for obtaining the required CLAR of all non-exempt human subject research and submitting the review to the RSRB when:

- Human subject research is conducted in a foreign country, unless conducted by a DoD overseas institution, or only involves DoD-affiliated personnel who are US citizens.
- The research requires a waiver of informed consent
- The research is fetal research
- Large-scale genomic data (LSGD) is collected from DoD-affiliated personnel.
- The research constitutes classified research involving human subjects.
- The research is required to be approved by the DOHRP (in addition to the COHRP).
- The research includes the use of a reliance agreement.

5.4. The RSRB is responsible for ensuring compliance with DoD regulatory requirements as indicated in Section 6.1 when the Reviewing IRB for research supported by DoD, or research that recruits DoD personnel. *Note:* The University of Rochester does not currently conduct classified research involving human subjects. Should this type of research be submitted to the RSRB, the RSRB will develop and utilize a checklist to document compliance with additional DoD requirements.

- When the RSRB is the Relying IRB, the RSRB will defer to the external IRB's DoD requirements consistent with the negotiated reliance agreement.

5.5. The RSRB is responsible for allowing authorized representatives of the DoD access to records that document compliance or noncompliance with this policy at reasonable times and in a reasonable manner.

5.6. When the RSRB is the Reviewing IRB, the RSRB is responsible for replacing the phrase "biomedical knowledge" with "generalizable knowledge" when applying sub-part B for DoD-supported research.

5.7. Civilian Investigators seeking to recruit military subjects are responsible for collaboration with a military researcher familiar with service-specific requirements.

5.8. For greater than minimal risk research involving DoD-personnel when recruitment and consent occur in a group setting, the Reviewing IRB will appoint an ombudsperson. The ombudsperson:

- Must not have a conflict of interest with the research or a member of the research team.
- Must be present during human participant 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.
- Should be available to address DoD-affiliated personnel's concerns about participation.

5.9. Investigators are responsible for notifying the DoD's Component Office of Human Research Protection (COHRP), within 30 days of the following, as applicable to both convened board and expedited reviews:

5.9.1. The Reviewing IRB has approved the research protocol and before the activities involving human subjects can begin (e.g., human subject recruitment and data collection) the COHRP must perform an administrative review of the research known as a Component Level Administrative Review (CLAR).

5.9.2. The CLAR Review must be conducted for any of the following:

- Human participant research is conducted in a foreign country, unless conducted by DoD overseas institution, or only involves DoD-affiliated personnel who are US citizens.
- The Involvement of DoD personnel in the conduct of the research is secondary to that of the non-DoD Institution.
- The research requires a waiver of informed consent.
- The research is fetal research.
- Large scale genomic data (LSGD) is collected from DoD-affiliated personnel. LSDG includes data derived from genome-wide association studies; single nucleotide polymorphisms arrays; genome sequencing; transcriptomic, metagenomic, epigenomic analyses; and gene expression data; etc.
- The research constitutes classified research involving human participants.
- The research is required to be approved by the DOHRP (in addition to the COHRP) in accordance with DoDI 3216.02.
- Component review includes review of reliance agreements.

5.9.3. Review and approval shall be based on confirmation that the research and non-DoD institution are in compliance with applicable regulations and policies, including any applicable laws and requirements and cultural sensitivities of a foreign country when the research is conducted in a foreign country.

5.9.4. The Reviewing IRB completes a continuing review.

5.9.5. Significant changes to the research protocol are approved by the Reviewing IRB.

- Changes to key Investigators or Institutions.
- Decreased benefit or increased risk to participants in greater than minimal risk research.
- Addition of vulnerable populations as participants.
- Addition of DoD-affiliated personnel as participants.

5.9.6. There is any change in the IRB of record.

5.9.7. Reports of audits of any component of the DoD-supported study by any federal department body, state agency, the official governing body of a Native American or Alaskan native tribe, other entity, or foreign government.

5.9.8. Any problem involving risks to participants or others, suspensions or termination of IRB approval, or any serious or continuing non-compliance.

5.9.9. Any unanticipated problems involving risks to participants or others and any subsequent action taken based on the findings.

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

5.9.11. Change in status when a previously enrolled participant becomes a prisoner, and the protocol was not reviewed and approved by the IRB in accordance with 32 CFR 219, Subpart C.

5.9.12. Closure of a DoD-supported study.

5.10. The Office of Research Project Administration (ORPA) is responsible for ensuring a formal agreement is established between organizations, specifying the roles and responsibilities of each party when conducting multi-site research.

6. Requirements

6.1. When the RSRB is the Reviewing IRB, during the process of initial and continuing review, the RSRB will:

6.1.1. Prohibit research involving the creation of a human embryo or embryos for research purposes, including gene editing research.

6.1.2. Prohibit research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of suffering, injury, or death greater than that allowed for research on fetuses in utero in accordance with Section 46.204(b) of Title 45, CFR, and Section 289g(b) of Title 42, U.S.C.

6.1.3. Prohibit research involving prisoners of war.

- This prohibition does not apply to activities covered by investigational new drug or investigational device provisions of FDA regulations, when the purpose is for diagnosis or treatment of a medical condition in a patient.
- Such treatment may be offered to detainees or prisoners of war with their informed consent when the medical products are subject to FDA regulations, and only when the same product may be available to DoD-affiliated personnel consistent with established medical practices.

6.1.4. Prohibit research involving the testing of chemical or biological agents.

6.1.5. Ensure scientific review is conducted according to Policy 505 Scientific Review Standards. As necessary, the RSRB may refer the scientific review back to the Investigator's department and/or outside consultation for additional expertise if necessary.

- During the process of reviewing amendments, the RSRB will perform scientific review on all substantive revisions to approved research.

6.1.6. During the process of initial review, determine if the research is intended to be beneficial to the subject. The RSRB will only permit consent to be obtained from a legally authorized representative when the research will benefit the subject.

6.1.7. The RSRB may consider the evaluation of minimal risk research, when applicable, in that the phrase does not include the inherent occupational risks that certain participants face in their everyday life, such as those:

- Encountered by Service members, law enforcement, or first responders while on duty.
- Resulting from or associated with high-risk behaviors or pursuits.
- Experienced by individuals whose medical conditions involve frequent tests or constant pain.

6.1.8. Determine if the consent form shall include disclosure of the provision for research-related injury for greater than minimal risk research:
- Consent documents must include the disclosure that participants may, for the duration of the study, be eligible for health care services for research-related injuries at a military treatment facility, and this eligibility for health care services extends beyond participants' participation in the study to such time after the study has ended.
- Consent documents must describe how the organizations will care for participants with research-related injuries, including injuries that are the direct result of activities performed by DoD-affiliated personnel in studies that are collaborative with non-DoD institutions.

6.1.9. Prohibit the exception from consent in emergency medicine research unless a waiver of advanced informed consent is obtained from the Secretary of Defense.

6.1.10. The RSRB may waive or alter some elements of informed consent for research involving human beings as experimental subjects so long as it preserves the informed consent of the participant (i.e., the consent indicates that participation is voluntary, and the participant/representative is informed of research risks.
- Informed Consent must be obtained prior to any research activity.
- If a subject is unable to provide informed consent and consent will be obtained from the subject's legal representative, the research must have a subject benefit.
- Waivers of consent are prohibited for DoD classified research.

6.2. The DoD Office for Human Research Protections (DOHRP) may waive the requirements for *prospective* consent for research involving a human being as an experimental subject when all the following are met:
- The research is necessary to advance the development of a medical product for the Military Services.
- The research may directly benefit the individual experimental subject.
- The research complies with all other applicable laws and regulations.
- If the research subject does not meet the definition of "experimental subject," the RSRB may waive the consent process without approval from the DOHRP.

6.3. When reviewing international research, require that the researcher obtain permission to conduct the research by certification or local ethics review, as per the Guideline for Conducting International Research. The researcher will also be required to provide the RSRB with an assurance that the proposed project will follows all local laws, regulations, customs, and practices.

6.4. Investigators are required to submit any surveys to be completed by DoD personnel to the DoD Information Management Control Officer (IMCO) for review and approval

after the research protocol is reviewed and approved by the Reviewing IRB, and before any recruitment of subjects. When a survey crosses DoD components, additional review is required.

- DoD-supported research reviewed using the expedited procedures, Investigators must follow the same reporting requirements described in section 5.8 of this policy.

6.5. 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.

6.6. When the RSRB is the Reviewing IRB, the RSRB will review Research Involving Genetics with *Policy 608 Research Involving Genetic Testing and Gene Transfer*

6.6.1. All studies involving LSGD collected on/from DoD-affiliated personnel will apply for a DHHS Certificate of Confidentiality (CoC).

- Any exceptions to the CoC must be listed in the consent form.

6.6.2. DoD administrative and DoD Component security reviews to ensure the adequacy of the proposed administrative, technical, and physical safeguards, including the secondary use or sharing of de-identified data or specimens must be conducted before research involving LSGD collected from DoD-affiliated personnel may begin.

6.6.3. Research involving LSGD from DoD-affiliated personal is subject to additional requirements (DoDI 3216.02 section 3.10):

- The disclosure of DoD-affiliated personnel's genomic data may pose a risk to national security; accordingly, written materials must describe administrative, technical, and physical safeguards commensurate with risk, including the secondary use or sharing of de-identified data or specimens.
- Must have a Certificate of Confidentiality from HHS.

6.7. When the RSRB is the Reviewing IRB, the RSRB will review non-compliance consistent with *Policy 802 Non-Compliance*.

6.7.1. When the RSRB determines that serious or continuing non-compliance has occurred in a DoD-supported study, the RSRB will report this to the DoD COHRP within 30 days of the RSRB determination according to the *Guideline for Institutional and Regulatory Reporting of Suspension, Termination, Non-Compliance and UPIRTSO.*

6.8. When the RSRB is the Reviewing IRB, the RSRB will review research events consistent with *Policy 801 Reporting Research Events* and the *Guideline for Reporting Research Events*.

6.8.1. When the RSRB determines that an unanticipated problem involving risk to subjects or others has occurred and any subsequent actions taken based on the findings in a DoD-supported study, the RSRB will report this to the DoD COHRP within 30 days of the RSRB determination according to the *Guideline for Institutional and Regulatory Reporting of Suspension, Termination, Non-Compliance and UPIRTSO*.

6.9. When the RSRB is the Reviewing IRB, the RSRB will report suspensions and terminations that occur in a DoD-supported study to the DoD COHRP within 30 days of the RSRB determination according to the *Guideline for Reporting Research Events* and the *Guideline for Institutional and Regulatory Reporting of Suspension, Termination, Non-Compliance and UPIRTSO*.

6.10. When the RSRB is the Reviewing IRB, the University of Rochester will review scientific misconduct consistent with UR *Policy on Research Misconduct* and, when scientific misconduct has occurred in a DoD-supported study, will report the incident to the DoD.

6.11. When the RSRB is the Reviewing IRB, the RSRB will utilize the *Checklist for RSRB Review of Research Supported by the DoD* (Appendix 1) to document compliance with DoD requirements listed within this policy.

7. Additional DoD Considerations for Research with Vulnerable Populations.

7.1. When reviewing research involving vulnerable populations, the RSRB will apply Department of Health and Human Services OHRP Subparts B, C, and D and the related OHSP policies and guidelines.

7.2. For human participant research that would not otherwise be approved but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates, written approval from the DOHRP must be obtained through the COHPR prior to research starting.

7.2.1. Ensure DoD-supported fetal research complies with Section 289g(b) of Title 42, U.S.C. and Subpart B of Section 46 of Title 45, CFR, as described in Paragraphs 3.1, 3.5, 3.6, and 3.9 of the DODI 3216.02.

7.2.2. 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 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.

7.2.3. 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.

7.3. For research conducted within the Bureau of Prisons, the additional protections outlined in *Policy 603 Research Involving Prisoners* will be applied.

7.3.1. In addition to the categories of permissible human participant research involving prisoners identified in DHHS regulations Subpart C, two additional categories are permissible (DoDI 3216.02 section 3.9 (c)):

1. Epidemiological research is permitted under the following conditions:
   - Where the sole purpose of the research is to describe the prevalence or incidence of a disease by identifying all cases, or study potential risk factor associations for a disease.
   - The research presents no more than minimal risk.
   - The research involves no more than inconvenience to the prisoner-participants.
   - Prisoners are not a particular focus of the research.
2. Human participant research involving prisoners that would otherwise meet exemption criteria may be conducted but must first be approved by the RSRB and meet the requirements of Subpart C and DoDI 3216.02.

7.3.2. DoD organizations conducting research involving prisoners must demonstrate to the senior designated official that the RSRB has fulfilled its duties in accordance with Subpart C.

7.3.3. When a previously enrolled human participant becomes a prisoner, and the protocol has not been reviewed and approved by the RSRB in accordance with Subpart C, the researcher must promptly notify the RSRB.

- For DoD-conducted research, the human protections director must notify the COHRP.
- For DoD-supported research, the RSRB must notify the DoD human research protection official DOHRPO and other federal agencies.
- The DOHRP must concur with the RSRB before the participant can continue to participate while a prisoner.

7.4. Service members and DoD-affiliated personnel are considered to be vulnerable to coercion and undue influence by the DoD due to the nature of the command structure of the organization. Therefore, additional protections for DoD-affiliated personnel are required, as follows:

7.4.1. In addition to the basic and required consent disclosures, consent documents for research that aim to enroll DoD-affiliated personnel must contain:

- A Statement that the DoD or a DoD organization is funding the study.
- A statement that representatives of the DoD are authorized to review research records.
- If the research includes any risks to their fitness for duty (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.
- The consent documentation must include, if applicable, potential risks for revocation of clearance, credentials, or other privileged access or duty.

7.4.2. If the research involves DoD-affiliated personnel, the researcher must receive Command or Component approval to conduct the research.

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

7.4.4. Military and civilian supervisors, officers, and others in the chain of command must not be present at any recruitment sessions or during the consent process.

- Excluded supervisors or those in the chain of command may participate in research, but must have separate recruitment sessions, if applicable.

7.4.5. Service members and all Reserve component and National Guard members in a federal duty status are considered 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 RSRB must carefully consider the research's recruitment process and the necessity of including such member as a human subject.

- When recruitment involves a percentage of a unit, an independent ombudsperson must be present.

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Revision History:

01/2015: Section 6.1.5 added to expand on definition of minimal risk per AAHRPP
06/2018: Section 3 – removed DoD Addendum definition; Section 4.1 removed DoD FWA reference; Section 4.2 added hyperlinks; Section 5 – removed responsibilities for DoD addendum and DoD training; Section 5.6, 6.1.8, 6.1.9 added to comply with new DoD requirements; added language throughout for Reviewing and Relying IRB; additional administrative changes
06/2020: Section 6.1.8 and section 6.1.9 revised wording; updated signatories
12/2024: Editorial revisions, updates; added Section 6.1.3, 6.1.4, 6.1.5 based on updated DoD regulations; updated signatories; removed appendix 1

Supersedes Date:

06/02/2020

Approved By:

Signed by:
Elizabeth Kipp Campbell
Signer Name: Elizabeth Kipp Campbell
Signing Reason: I approve this document
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12/6/2024 | 4:28:40 PM EST

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49FD24DE73D54EC683859794C6848D96

12/6/2024 | 6:30:01 PM EST

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12/8/2024 | 10:17:31 AM PST

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