Wright State IRB Guidance: Additional Requirements for Research Involving the Department of Defense

Human subject research that is sponsored by the Department of Defense (DoD), involves collaboration with DoD or involves DoD facilities or personnel (military or civilian), is subject to additional requirements. These regulatory requirements include special subject protections, as well as additional review and reporting requirements for investigators and the Wright State IRB or external IRB of record. Investigators should review these requirements when planning a DoD-supported research project as they may add a significant amount of time to the review and approval process of such research.

The purpose of this document is to provide investigators with guidance on how to comply with the requirements outlined in DoD Instruction 3216.02 (DoDI 3216.02), Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research (April 15, 2020).

Each DoD Component (e.g., Army, Navy, Air Force) may have additional requirements beyond those included in this guidance document. Investigators are advised to check with their sponsoring Component program manager about any additional requirements.

List of DoD Components

DoD Components include, but may not be limited to:

- Navy
- Office of Naval Research
- Naval Academy
- U.S. Naval Observatory
- Army
- U.S. Army Corps of Engineers
- Coast Guard Academy
- Military Academy (West Point)
- Air Force
- Air Force Academy
- Marines
- Coast Guard

Single IRB Requirement

The DoD requires the 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 (COHRP) 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 context of the proposed research. Studies already in progress before January 20, 2020, will not be required to transition to a single IRB, nor submit exception documentation.

If reliance on an IRB other than the Wright State IRB is required, investigators are also required to comply with the submission requirements described in the *Collaborative Research and External Reliance Policy.*

When do the DoD Special Requirements Apply?

Human research must comply with DoD requirements when:

- The research is funded by a DoD Component, including cases where Wright State is the recipient of a subaward from the direct recipient of DoD funds, or
- The research involves cooperation, collaboration, or other type of agreement with a DoD Component, or
- The research uses property, facilities, or assets of a DoD Component, or
- The subject population will intentionally include personnel (military and/or civilian) from a DoD Component. (DoD requirements do not apply when DoD personnel incidentally participate in research where they are not the intended research population or where the project is not DoD-supported).

Prohibited Research

The following describes types of DoD-related human subject research that are prohibited at Wright State:

- Research with detainees or prisoners of war, except research with investigational new drugs or devices when the purpose is for diagnosis or treatment of a medical condition in a patient, with their informed consent, and where such treatment would also be offered to US military service members at the same location and with the same medical condition consistent with established medical practice. DoD Instruction 2310.01E defines a detainee as: "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."
- Classified research, and
- Human testing of chemical or biological agents, except for certain prophylactic, protective or peaceful purposes.

DoD Human Research Protections Office (HRPO) Required Reviews and Reporting

<u>Initial Review</u>

Upon completion of Wright State IRB review and approval (including exemption or not human subject research determinations), the HRPO for the sponsoring Component (e.g., Army, Navy,

Air Force) must perform an administrative review of the research before activities with research subjects may begin. The review involves confirmation that Wright State and the proposed research are in compliance with DoD requirements.

If research will be conducted in a foreign country, the administrative review will also ensure compliance with any applicable laws and requirements and cultural sensitivities of a foreign country. While the HRPO review is not an IRB review, the HRPO may require changes to the research prior to the start of the research. The Principal Investigator is responsible for submitting any changes required by the sponsoring Component to the IRB of record for review and approval prior to implementation. It is important for investigators to plan for this part of the approval process as it may require a considerable amount of time and effort.

Required Reporting to the HRPO During Conduct of Research

The following must be promptly reported to the HRPO (generally within 30 days of the event):

- IRB-approved changes to 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.
- Transfer of research oversight to a different IRB.
- 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 research is under investigation.
- Any problems involving risks to subjects or others, suspension, or termination of IRB approval, or any serious or continuing noncompliance pertaining to DoD-supported research.
- The results of the IRB's continuing review, if required.
- 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 of 45 CFR 46.
- 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 of 45 CFR 46, and
- A DoD-supported study's closure.

DoD Definitions of Experimental Subjects and Minimal Risk

10 USC 980 provides a special definition for *experimental subjects* as those included in "an activity, for research purposes, where there is intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or

interaction." Examples of interventions or interactions include, but are not limited to, a physical procedure, a drug, a manipulation of the subject or the subject's environment or the withholding of an intervention that would have been undertaken if not for the research.

The definition of minimal risk that includes the phrase "ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests" must not be interpreted to include the inherent risks that certain individuals face in their everyday lives, 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.

Investigator Training Requirements

DoD requires that key investigators complete human research protections training. There might be specific DoD educational requirements or certification required by different DoD components. Key investigators are defined as "persons leading the performance of research." Wright State's CITI Human Subjects Research training, renewable every three years, meets the training requirements for many DoD Components but may not cover all required training. The Principal Investigator (PI) is responsible for ensuring that all study team members engaged in the conduct of research complete the required training. The DoD Component may evaluate Wright State's human research training requirements to ensure that personnel are qualified to perform the research, based upon the complexity and risk of the research.

Scientific Review Requirements

The IRB must consider the scientific merit of the research during their review. The IRB may rely on outside experts to provide an evaluation of scientific merit. The scientific review may be the review provided by the funding agency (including DoD), by an established internal review mechanism in the researcher's academic unit, or in the form of an ad hoc review by the investigator's chair or dean. In some cases, the evaluation of scientific merit that is conducted by the IRB as part of its review is sufficient. The IRB or DoD program manager can assist with the determination of the appropriate review mechanism.

If required, documentation of the scientific review must be provided to the IRB at the time the IRB application is submitted and for substantive amendments. Scientific review must demonstrate that the research uses procedures consistent with sound research design and is likely to yield the expected results and should include the assessment of the following elements:

- Significance of the research question;
- Scientific approach;
- Research team qualifications; and
- Facilities and resources available.

The name and qualification of the reviewer(s) should be included as part of the review.

Independent Medical Monitor

For research involving more than minimal risk (as defined in 32 CFR 219.103(i)), an independent medical monitor must be appointed by name in the IRB study application. Medical monitors should be physicians, dentists, psychologists, nurses, or other healthcare providers capable of overseeing the progress of research protocols, especially issues of individual subject management and safety. The medical monitor must be independent of the study team and must have attained sufficient educational and professional experience to serve as the subject advocate. It is the PI's responsibility to include a detailed monitoring plan with the initial IRB submission.

Depending on the nature of the research, the medical monitor may be assigned to one or more phases of the study (e.g., recruitment, data analysis). In accordance with the IRB-approved monitoring plan, the medical monitor may discuss the research with the PI, interview subjects, consult on individual cases, or evaluate reportable events reports. The medical monitor must agree to promptly report any discrepancies or problems to the IRB. He/she should also have the authority to stop the study, withdraw individual subjects, and take whatever steps are necessary to protect the safety and wellbeing of study subjects until the IRB can assess the monitor's report.

Additional Required DoD Approval of Surveys/Interviews

Research involving surveys or interviews with DoD personnel (military or civilian) or their families may require DoD approval after the research protocol is reviewed and approved by the IRB. When a survey crosses DoD Components, additional review is required. The DoD Component program manager can confirm any additional review requirements and the timing of the review (before or after IRB review). Documentation of this review must be provided to the Wright State IRB Office by the PI.

International Research Requirements

In its review of research conducted outside of the United States, the IRB must confirm that all national laws and requirements of the foreign country have been met and consider the cultural sensitivities in the setting where the research will take place. The investigator must obtain

permission to conduct research in that country by written certification or local ethics review and follow all local laws, regulations, customs, and practices.

Requirements When DoD Affiliated Personnel are Research Subjects

DoD Affiliated Personnel means service members, reserve service members, National Guard members, DoD civilians, and DoD contractors. 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 research recruitment process and the necessity of including such member as a human subject.

If the research involves DoD-affiliated personnel as subjects and 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.

If the research involves DoD-affiliated personnel, the principal investigator must receive command or Component approval to execute the research.

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

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

For greater than minimal risk research and where recruitment is conducted in a group setting, the IRB must appoint an ombudsman person. The ombudsperson:

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

Limitations on Subject Compensation

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.

Informed Consent

Requirements and Elements

For the IRB to approve research involving DoD-affiliated personnel as human subjects the consent documentation must include, if applicable, potential risks for the revocation of clearance, credentials, or other privileged access or duty.

Consent documents must also include the following additional DoD elements of disclosure:

- A statement that the DoD or a DoD organization is funding the study unless the research involves no more than minimal risk. The Secretary of Defense may grant an exception to this requirement on the grounds that providing this information could compromise intelligence sources or methods.
- A statement that representatives of the DoD are authorized to review research records.
- The disclosure for research-related injury must follow the requirements of the DOD component.

DoD Limitations on Waivers of Informed Consent and Consent by LARs

For any research using DoD funds that also meets the definition of research involving a human being as an experimental subject (see above) the requirement to obtain consent cannot be waived by an IRB of record. This prohibition may limit an investigator's ability to conduct such research if it involves deception, decisionally impaired individuals, or research being conducted under emergency conditions where a subject may not be able to provide consent.

When the research meets the 10 USC 980 definition of research involving a human being as an experimental subject, informed consent must be obtained in advance from the subject or the subject's legal representative consistent with the Common Rule if the participant cannot consent. Informed consent may be provided by a legally authorized representative (LAR) only if: (1) the research participant lacks decision-making capacity; AND (2) the IRB has determined that the research is intended to be beneficial to the individual research subjects.

This statute applies only to certain intervention studies. It does not apply to retrospective research involving analysis of data or specimens, observational studies, blood draws, or tissue collection, and does NOT apply to screening of records to identify possible research subjects. The IRB may grant a waiver of consent for such activities.

The Secretary of Defense may waive this consent requirement for a specific project to advance the development of a medical product necessary to the Armed Forces, but only if the research may directly benefit the research participant and the research is carried out in accordance with all other applicable laws and regulations.

Certificates of Confidentiality

A Certificate of Confidentiality (CoC) 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.

A DoD institution conducting human subject research or non-DoD institution conducting human subject research with DoD support may request a CoC pursuant to Section 241 of Title 42, U.S.C. All studies involving large scale genomic data (LSGD) collected on DoD-affiliated personnel (described on page 9) will apply an HHS CoC.

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

Research Involving Vulnerable Populations

Pregnant Women/Fetuses

DoD requires that the protection of Common Rule Subpart B (Pregnant Women/Fetuses), C (Prisoners), and D (Children) be applied to the research it supports. The DoD (and the IRB) considers the need for similar safeguards for other vulnerable populations such as those with cognitive impairment, mental illness, physical disability, or any other circumstance that might require special protections.

For research involving pregnant women, fetuses, and neonates as subjects:

- For purposes of applying Subpart B, the phrase “biomedical knowledge” is replaced with “generalizable knowledge.”
- The applicability of Subpart B is limited to research involving pregnant women as participants in research that is more than minimal risk and includes interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as subjects.
- Research using fetal tissue must comply with US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g – 289g-2.

Prisoners

In addition to allowable categories of research on prisoners identified in Subpart C, two additional categories are permissible:

- 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, DoD requirements, and other applicable requirements.
- Human subjects 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, DoD requirements, and other applicable requirements.

When a previously enrolled subject becomes a prisoner and the relevant research protocol was not reviewed and approved by the IRB in accordance with Subpart C of 45 CFR 46, the principal investigator must promptly notify the IRB. For DoD supported research, the non-DoD institution must notify the HRPO and other federal agencies, if required.

Children

Research involving children must meet the additional relevant protections of Subpart D. The exemption of research involving survey or interview procedures or observation of public behavior, does not apply to research with children, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

Research Involving Large Scale Genomic Data (LSGD) Collected on DoD-Affiliated Personnel

LSGD is data derived from genome-wide association studies; single nucleotide polymorphisms arrays; genome sequencing; transcriptomic, metagenomic, epigenomic analyses; and gene expression data; etc. Research involving LSGD may or may not also constitute human subject research. 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.

DoD-conducted or DoD-supported research involving LSGD collected on DoD-affiliated personnel, or for which research the DoD provides assistance, is subject to additional requirements:

- 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.

- All research involving LSGD collected from DoD-affiliated personnel will apply an HHS Certificate of Confidentiality pursuant to Title 42, U.S.C., and Public Law 114-255. Research involving LSGD 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.

Recordkeeping Requirements

Consistent with Wright State policy, research records must be maintained for at least 3 years after the completion of the research. The DoD may require that research records be transferred to the DoD Component rather than being retained by Wright State.

Records that document compliance or noncompliance with DoD regulations must be made accessible for inspection and copying by authorized representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD Component.

References

The DoD regulatory and guidance resources listed here are key resources regarding the conduct of DoD-related human subject research. This section is not intended to serve as an all-encompassing list of all regulations or guidance that may apply to such research. The sponsoring DoD Component can provide additional information:

- 32 CFR 219, Protection of Human Subjects
- 10 USC 980, Limitations on the Use of Humans as Experimental Subjects
- DoD Instruction 3216.02, Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research
- DoD Instruction 3210.7 Research Integrity and Misconduct
- DoD Instruction 6200.2, Use of Investigational New Drugs in Force Health Protection
- Air Force Instruction DODI3216.02_AFI40-402: Protection of Human Subjects and Adherence to Ethical Standards in Air Force Supported Research.