U.S. Army Medical Research and Development Command
Office of Research Protections
Human Research Protection Office

DOD Instruction (DODI) 3216.02, "Protection of Human Subjects and Adherence to Ethical Standards in DoD-Conducted and - Supported Research," Issued April 15, 2020: Summary of Requirements for DOD-supported Research

Background: All U.S. Army Medical Research and Development Command (USAMRDC) supported/funded research involving human subjects, human data, or human specimens must be reviewed for compliance with Federal, Department of Defense (DOD), and Army human subjects protection requirements and receive approval by the Office of Research Protections (ORP) Human Research Protection Office (HRPO) prior to implementation; this requirement derives from DODI 3216.02 and the Defense Federal Acquisition Regulation Supplement. On 15 April 2020, the DOD issued an update to DODI 3216.02.

Purpose: This document compares the previous and new DODI 3216.02's requirements for non-DOD institutions receiving DOD support for activities that include (or may include) human subjects research, and provides information on how the USAMRDC ORP HRPO implements the DODI requirements.

DODI 3216.02 Submission Requirements: Prior to HRPO Initial Approval		
Non-exempt human subjects research		**USAMRDC ORP HRPO Comments/Clarifications**
<u>Previous</u> DODI	**<u>Current</u> DODI** ***For DOD-supported, non-exempt human subjects research, the awardee institution must <u>submit to the HRPO:</u>***	
IRB review documentation: the HRPO must: Review the research protocol and accept the IRB determination of level of risk and approval of the study for compliance with [the DODI].	IRB review documentation: Documentation that the DOD-supported human subjects research has been reviewed and approved by an IRB . . . IRB-approved protocol documents.	Single IRB review required for multi-site, collaborative research in accordance with section .114 of the Common Rule for research conducted within the U.S. See guidance and submission forms at the ORP HRPO website: https://mrdc.amedd.army.mil/index.cfm/collaborate/research_protections/hrpo

DODI 3216.02 Submission Requirements: Prior to HRPO Initial Approval		
Non-exempt human subjects research		**USAMRDC ORP HRPO Comments/Clarifications**
<u>Previous</u> DODI	**<u>Current</u> DODI** ***For DOD-supported, non-exempt human subjects research, the awardee institution must <u>submit to the HRPO:</u>***	
Scientific merit: When conducting non-exempt human subjects research, the IRB review must consider the scientific merit of the research. The IRB may rely on outside experts to provide an evaluation of the scientific merit.	Scientific merit: Documentation that the DOD-supported human subjects research has been reviewed and approved by an IRB, including scientific merit . . .	
Education and Training: [The HRPO must] evaluate the non-DOD institution's education and training policies to ensure the personnel are qualified to perform the research. The rigor of the evaluation should be appropriate for the complexity and risk of the research.	Education and Training: Documentation of key investigators' human research protection training.	ORP HRPO requires documentation of current human subjects protection training for the Principal Investigator and all Associate Investigators named on the protocol.
Assurance: At a minimum, the HRPO must confirm the non-DOD institution has a Federal assurance appropriate for the research in question.	Assurance: Current Federalwide Assurance (FWA) and IRB registration numbers.	All non-DOD institutions (both U.S. and international sites) whose employees interact/intervene with research subjects or their identifiable data must have an approved FWA. Additional information available at the ORP HRPO website: https://mrdc.amedd.army.mil/index.cfm/collaborate/research_protections/hrpo

DODI 3216.02 Submission Requirements: Prior to HRPO Initial Approval		
Exempt human subjects research and research not involving human subjects		**USAMRDC ORP HRPO Comments/Clarifications**
<u>Previous</u> DODI	**<u>Current</u> DODI** ***For DOD-supported, non-exempt human subjects research, the awardee institution must <u>submit to the HRPO</u>:***	
Institutional Determinations: When the contract or other agreement may include research involving human subjects and if the non-DOD institution determines either the activity is **not research involving human subjects or is exempt** research involving human subjects, the HRPO must concur with the performing institution's determination before activity can begin.	Institutional determinations: For DOD-supported research that is **exempt or does not involve human subjects** the awardee institution <u>must submit</u> to the HRPO institutional documentation of the determination that the research is either not human subjects research, exempt human subjects research, or limited IRB review, to include all protocol documents.	See guidance and submission forms at https://mrdc.amedd.army.mil/index.cfm/collaborate/research_protections/hrpo

DODI 3216.02 Submission Requirements: After HRPO Approval		
<u>Previous</u> DODI	**<u>Current</u> DODI** ***The non-DOD institution must <u>promptly notify</u> the HRPO of:***	**How Defined/Implemented by the USAMRDC ORP HRPO:**
The HRPO must . . . review and accept IRB-approved substantive changes to an approved research protocol before they are implemented. The non-DOD institution must promptly notify the HRPO of the following: when significant changes to the research protocol are approved by the IRB, . . . if the IRB used to review and approve the research changes to a different IRB . . .	IRB-approved changes to human subjects 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.	Substantive modifications to the research protocol and any modifications that could potentially increase risk to subjects must be submitted to the HRPO for approval prior to implementation. The USAMRDC ORP HRPO defines a substantive modification as a change in Principal Investigator, change or addition of an institution (Note: HRPO review and approval of institution is required.), change to the IRB of Record, elimination or alteration of the consent

DODI 3216.02 Submission Requirements: After HRPO Approval		
Previous DODI	**Current DODI** ***The non-DOD institution must promptly notify the HRPO of:***	**How Defined/Implemented by the USAMRDC ORP HRPO:**
	Transfer of human subjects research oversight to a different IRB.	process, change to the study population that has regulatory implications (e.g. adding children, adding active duty population, etc.), significant change in study design (i.e. would prompt additional scientific review), or a change that could potentially increase risks to subjects.
The HRPO must . . . ensure the IRB conducts an appropriate continuing review at least annually.	The results of the IRB's continuing review, if required.	A copy of the IRB continuing review approval letter, submitted to the ORP HRPO as soon as possible after receipt of approval (if applicable).
Not specifically addressed.	A DOD-supported study's closure.	The final study report submitted to the IRB, including a copy of any acknowledgement documentation and any supporting documents, submitted to the ORP HRPO as soon as all documents become available.

DODI 3216.02 Prompt Reporting Requirements		
Previous DODI	**Current DODI** ***The non-DOD institution must promptly notify the HRPO of:***	**As Defined/Implemented by the USAMRDC ORP HRPO** ***The following study events must be promptly reported to the HRPO:***
The non-DOD institution must promptly notify the HRPO of the following: . . . when the institution is notified by any Federal department or agency or national organization that any part of its HRPP is under investigation for cause involving a DOD-supported research protocol, and all UPIRTSOs, suspensions, terminations, and serious or continuing noncompliance regarding	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 subjects research is under investigation.	The knowledge of any pending compliance inspection/visit by the Food and Drug Administration (FDA), Office for Human Research Protections, or other government agency concerning this clinical investigation or research. The issuance of inspection reports, FDA Form 483, warning letters, or actions taken by any government regulatory agencies.

DODI 3216.02 Prompt Reporting Requirements		
<u>Previous</u> DODI	**<u>Current</u> DODI** ***The non-DOD institution must <u>promptly notify</u> the HRPO of:***	**As Defined/Implemented by the USAMRDC ORP HRPO** ***The following study events must be <u>promptly reported</u> to the HRPO:***
DOD-supported research involving human subjects.	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 subjects research.	All unanticipated problems involving risk to subjects or others (UPIRTSOs). Suspensions, clinical holds (voluntary or involuntary), or terminations of this research by the IRB, the institution, the sponsor, or regulatory agencies. Any instances of serious or continuing noncompliance with the federal regulations or IRB requirements.
	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.	Change in subject status when a previously enrolled human subject becomes a prisoner must be promptly reported to the USAMRDC ORP HRPO. The report must include actions taken by the institution and the IRB.

Additional Requirements		
<u>Previous</u> DODI	**<u>Current</u> DODI** ***The non-DOD Institution must also:***	**Comments/Clarifications**
Records maintained by non-DOD institutions that document compliance or noncompliance with [the DODI] shall 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.	Make records that document compliance or noncompliance with DODI 3216.02 accessible for inspection and copying, as determined by DOD HRPP personnel, by authorized DOD representatives.	Essentially unchanged from previous DODI. The ORP HRPO may conduct random or for-cause audits or site visits and require access to records. This DODI requirement is the basis for requiring information in the informed consent document to inform subjects that the DOD may have access to identifiable records.
The non-DOD institution shall comply with the terms of the DFARS clause or comparable language used in the agreement with the DOD Component supporting the research involving human subjects . . .	Recognize that failure to comply with applicable requirements may result in the DOD: a. Wholly or partially terminating or suspending the award; b. Temporarily withholding payment under the award pending correction of the deficiency; c. Disallowing all or part of the cost of the activity or action that is not in compliance; and/or d. Contacting publishers of articles that reference the noncompliant human subjects research.	See acquisition regulations (DFARS clause 252.235-7004) and terms of award
Non-DOD institutions shall comply with requirements of this Instruction applicable to them.	Recognize that DOD-supported research should comply with the whole of DODI 3216.02 when applicable.	
No comparable requirement.	Promptly notify the HRPO of change in status when a previously enrolled human subject becomes pregnant, or when the researcher learns that a previously enrolled human subject is	The ORP HRPO implements this element by requiring the prompt reporting of all UPIRTSOs. Only on-study pregnancies that also constitute a UPIRTSO (as determined by the reviewing

Additional Requirements		
Previous DODI	**Current DODI** ***The non-DOD Institution must also:***	**Comments/Clarifications**
	pregnant, and the protocol was not reviewed and approved by the IRB in accordance with Subpart B, Subpart 46 of Title 45, CFR.	IRB) require prompt reporting to the ORP HRPO.

Also new with the April 2020 version:

- **Research Monitor.** The prior DODI 3216.02 required that Institutional Review Boards (IRB) approve an independent Research Monitor with specific roles and responsibilities for all greater than minimal risk studies supported by the DOD. The revised DODI no longer includes this requirement.

- **DOD IRB review in lieu of HRPO.** When a DOD IRB serves as the reviewing IRB for a non-DOD institution, the DOD IRB approval will constitute the HRPO review; an additional HRPO review is not required. USAMRDC-supported non-DOD institutions that rely on a DOD IRB for review must still provide certain materials to the ORP HRPO for review and issuance of a written approval, in accordance with the support agreement. The ORP HRPO has developed a specific submission form for use by non-DOD institutions that rely on a DOD IRB, available at the HRPO website: https://mrdc.amedd.army.mil/index.cfm/collaborate/research_protections/hrpo

- **Large Scale Genomic Data.** Additional reviews (i.e., DOD administrative and DOD Component security reviews) must be conducted before research involving large scale genomic data collected from DOD-affiliated personnel may begin.