

Department of Defense (DoD) Requirements for Human Subjects Research

Introduction

The purpose of this module is to explain the unique requirements applicable to DoD human subject research. The DoD and 17 other Federal departments and agencies that support human subject research follow the requirements of the “Federal Policy for the Protection of Human Subjects,” also known as the Common Rule. The Department of Defense’s regulation pertaining to the Common Rule, Subpart A is cited at [32 Code of Federal Regulations \(CFR\) 219](#).

This module presumes the reader already understands the requirements and ethical implications of the Common Rule and the additional requirements described at [45 CFR 46, subparts B-D](#). If you are not familiar with these policies, please complete the CITI modules relevant to these topics before proceeding with this module.

In this module, the words “Command” and “institution” may refer to the investigator, the Institutional Official (IO), the Institutional Review Board (IRB), the Human Protections Administrator (HPA), or other person representing the institution. This module does not include every DoD requirement a Command/institution must follow; this module is not a replacement for [DoD Instruction \(DoDI\) 3216.02](#) and other applicable Federal policies.

This module identifies and explains the significant policy requirements in DoDI 3216.02 that apply to Department of the Navy (DON) human subject research. Secretary of the Navy Instruction (SECNAVINST) 3900.39D currently describes and defines DON policy, which is implemented by the DON Human Research Protection Program (HRPP).

Learning Objectives

By the end of this module, you will be able to:

- Describe at least three unique DoD requirements for human subjects research
- List two requirements that institutions must address when appointing a research monitor

DoD Requirements for Human Subjects Research

In addition to 50 U.S. Code 1520a regarding chemical and biological research and DoDI 3216.02 requirements for research with classified information, Federal Departments and agencies also must comply with the requirements discussed in this module:

1. Applicability of DoDI 3216.02 and the Common Rule
2. Approval of the Research Protocol
3. Expedited Review Category 5

4. Research Monitor for Greater Than Minimal Risk Research
5. Research Involving a Human Being as an Experimental Subject
6. Selection of Human Subjects and Evaluating Risk
7. DoD Personnel as Subjects
8. Compensation to Federal Personnel as Human Subjects for their Participation
9. Research Conducted in a Foreign Country
10. Pregnant Women, Fetuses, Neonates as Subjects
11. Prisoners as Subjects
12. Disclosure of Provision for Medical Expenses if Injured

DoD-Unique Requirements

DoDI 3216.02 identifies how the DoD will comply with the Common Rule mandate to protect human subjects. References are cited in this module, as well as the DON and other DoD Component policies that implement DoDI 3216.02.

1 Applicability of DoDI 3216.02 and the Common Rule

DoDI 3216.02 applies to:

- a. 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 DoD.
- b. All DoD-conducted or -supported research involving human subjects as defined in the Glossary of DoDI 3216.02. All such activities must include both systematic investigation designed to develop or contribute to generalizable knowledge AND involve a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or about whom identifiable private information is obtained.
- c. Activities such as research, development, testing, and evaluation (RDT&E) that meet the definition of research involving human subjects (as defined in the Glossary of DoDI 3216.02), as well as clinical investigations or medical activities regulated by the Food and Drug Administration (FDA) in parts 50, 56, 312, 600, and 812 of title 21, CFR.

DoD-supported research means research involving human subjects for which the DoD provides any resources to conduct the research. Resources may include but are not limited to funding, facilities, equipment, personnel (investigators or other personnel performing tasks identified in the research protocol), access to or information about DoD personnel for recruitment, or identifiable data or identifiable specimens from living individuals and cadaver data linked to living individuals.

2 Approval of the Research Protocol

Investigators should follow the policies of their Command or institution to determine if the proposed research meets the Common Rule definition of: 1) “research,” 2) “involving a human subject,” and 3) if the human subject research meets any of the criteria at 32 CFR 219.101(b) for exemption from IRB review. DON IRB approval must be obtained before any activities that involve human subjects research can begin.

DON Commands and institutions engaged in non-exempt research involving human subjects and collaborating with a non-DoD institution may rely on a collaborating non-DoD institution’s IRB if these minimum conditions are met:

- a. The collaborating non-DoD institution has an appropriate Federal Assurance.
- b. The involvement of DON personnel in the conduct of the research involving human subjects is secondary to that of the non-DoD institution.
- c. The DON Command/institution, the non-DoD institution, and the non-DoD institution’s IRB have a written agreement defining the responsibilities and authorities of each organization in complying with the terms of the Federal Assurances and DoDI 3216.02 (i.e., have an Institutional Agreement for IRB Review or similar agreement). DON HRPP shall approve the terms of the agreement prior to the DoD institution’s engagement in the research involving human subjects.
- d. DON HRPP or designated Command/institution officials must conduct an appropriate administrative review of the research involving human subjects to ensure it complies with DoD and DON policies and procedures prior to the DON Command/institution’s engagement in the research.

3 Expedited Review Category 5

DoD allows the use of expedited review for the nine research categories as described in the [Federal Register \(FR\) Notice](#) (63 FR 60364-60367, November 9, 1998). For research category 5, DoDI 3216.02 allows IRBs to use expedited review procedures under 32 CFR 219.110(a) to review minimal risk, non-exempt human subject research using materials (e.g., data, documents, records, or specimens) that previously have been collected for any purpose, provided the materials were not collected for the currently proposed research.

4 Research Monitor for Greater Than Minimal Risk Research

For human subject research that involves greater than minimal risk, the IRB shall approve an independent research monitor by name. There may be more than one research monitor for a single research protocol. The monitor may be an ombudsman or a member of the data safety monitoring board.

A written summary of the research monitor’s duties shall be approved by the IRB based on the specific risks or concerns about the research. The research monitor may perform

oversight functions (e.g., observe recruitment, oversee study interventions and interactions, review monitoring plans and reports of unanticipated problems involving risks to subjects or others [UPIRTSOs], and oversee data matching) and report their observations and findings to the IRB or a designated official.

The research monitor shall have authority to stop a research protocol in progress, remove individual human subjects from a research protocol, and take whatever steps are necessary to protect the safety and well-being of human subjects until the IRB can assess the monitor's report.

The investigator may request a waiver of the requirement for the research monitor when the inclusion of a research monitor does not add protections for human subjects. The Navy Surgeon General may waive the requirement for a research monitor on a case-by-case basis when a monitor is not necessary to provide additional protections for human subjects.

5 Research Involving a Human Being as an Experimental Subject

DoDI 3216.02 explains the requirements of Section 980 of Title 10 USC regarding the limitation of the IRB's ability to waive informed consent. DoDI 3216.02 defines "research involving a human being as an experimental subject," as "an activity for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction." This differs from the Common Rule use and definition of "research involving a human subject." Research involving a human being as an experimental subject is not applicable to activities that are considered solely medical treatment, medical practice, or medical compliance monitoring activities, or activities that are exempt under 32 CFR 219.

When conducting research involving a human being as an experimental subject, the investigator must obtain consent from the experimental subject. Consent can be obtained from the subject's legally authorized representative only if the research is intended to be beneficial to the subject. The criteria for waiving informed consent are described in DoDI 3216.02. Requests for waivers must be submitted to DON HRPP.

6 Selection of Human Subjects and Evaluating Risk

The selection of human subjects reflecting gender and minority participation in DoD-conducted or -supported clinical research involving human subjects shall comply with Section 252 of Public Law 103-160.

When evaluating the risk of research, IRB shall not interpret the phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests" in the definition of minimal risk (section 219.102(i)) to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special

population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

7 DoD Personnel as Subjects

Usually a letter of support is needed from the Commander of the DON Command/institution in which recruitment will occur or the research will be conducted. In some cases, DoD personnel may be required to seek written permission from their supervisor prior to participation as subjects in research studies.

Superiors (e.g., military and civilian supervisors) are prohibited from influencing the decisions of their subordinates (e.g., junior enlisted personnel) regarding participation as subjects in research. Letters of support for the research must not contain language that could reasonably be considered undue influence on a person's decision to volunteer. To reduce undue influence, recruitment sessions shall not occur as part of activities that include mandatory attendance, e.g., official meetings, briefings, Commander's Calls, etc.

Superiors in the chain of command shall not be present at any human subject recruitment sessions or during the consent process in which members of units under their command are afforded the opportunity to participate as human subjects. Superiors can be given an opportunity to participate as human subjects in a separate recruitment session.

For research involving military personnel 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 with the research and shall be present during the recruitment in order to monitor that the voluntary involvement or recruitment of the military is clearly and adequately stressed and that the information provided about the research is clear, adequate, and accurate. When an ombudsman is not required for recruiting military and DoD employees, the IRB should consider the subject population, the consent process, and the recruitment strategy to determine if it is appropriate to appoint an ombudsman.

When assessing the level of risk to military and DoD employees as subjects, the investigator and IRB need to consider unique DoD and Federal policies. Privacy and confidentiality risk assessment for military personnel requires serious consideration of the potential impact on a military career. For example, information could impact future job placement, and some medical and psychological information could lead to limitation of duties or discharge from the military. Information about alcohol or drug abuse, drunk driving, and sexual or spousal abuse could lead to loss of a career or pay for both military and DoD personnel or have other ramifications.

For the purposes of legal capacity to participate in human subject research, all active duty U.S. Service members and all Reserve Component members in a Federal duty status are considered adults. The participation of such members in human subject research is not subject to requirements of 45 CFR 46, subpart D. However, when such military members

are under 18 years of age, students at Service Academies, or trainees, the IRB shall carefully consider the recruitment process and the necessity to include such members as human subjects (even though the requirements in subpart D do not apply).

8 Compensation to Federal Personnel as Human Subjects for their Participation

Three key factors determine whether subjects may be compensated for participating in research.

- a. Are the potential subjects Federal personnel (military or civilian)?
- b. If the subjects are Federal personnel, are they participating in an on-duty or off-duty status?
- c. Are the funds used to pay the subjects coming directly from a Federal source?

When subjects are Federal personnel (military and civilian) and on-duty, compensation is limited to no more than \$50 per blood draw. On-duty personnel cannot be paid for any research activities other than blood draws.

When subjects are Federal personnel (military and civilian) and off-duty, they may receive up to \$50 for each blood draw. Additionally, Federal personnel while off-duty may be compensated for research participation other than blood draws in the same way as human subjects who are not Federal personnel as long as federal funds are not the direct source of compensation (and compensation is approved by an IRB as being non-coercive and not represent an undue influence per 32 CFR 219.116).

When subjects are not Federal personnel, they may receive up to \$50 for each blood draw. Non-Federal personnel may be compensated for research participation other than blood draws in a reasonable amount as approved by the IRB according to prevailing rates and the nature of the research. Payment for participation may come directly from a Federal or non-Federal source.

9 Research Conducted in a Foreign Country

When the research is conducted in a foreign country whose laws and regulations are applicable to that research, the IRB shall confirm that, in addition to the Common Rule and DoD Instruction 3216.02, all applicable requirements of the foreign country have been met. The IRB also shall consider the cultural sensibilities of the setting where the research will take place. In the event of an unresolved conflict between the foreign country's requirements and those of the Common Rule and DoDI 3216.02 such that compliance with all is impossible, the institution must seek guidance from DON HRPP.

At a minimum, the DON must conduct an administrative review and approve all research involving non-exempt human subjects approved by a DoD institution when any of these conditions occur:

a. The research will be conducted in a foreign country unless either:

(1) The research will be conducted by an established DoD overseas research institution and the research will be conducted in the host country, or

(2) The research will be conducted by a DoD overseas institution and will include only DoD personnel or U.S. citizens as human subjects.

b. The research involves a collaboration with a non-DoD institution and the DoD institution is relying on the non-DoD institution's IRB, which is not composed of Federal employees.

c. The research permits a waiver of informed consent under paragraph (b) of Section 980 of Title 10, USC.

d. The research involves any fetal research covered under sections 289g–289g-2 of Title 42, USC.

e. The research requires approval by either the ASD(R&E) or the Head of the OSD or DoD Component as delegated by the ASD(R&E).

10 Pregnant Women, Fetuses, and Neonates as Subjects

Non-exempt research involving pregnant women, fetuses, or neonates as human subjects must meet the additional relevant protections of 45 CFR 46, subpart B, as modified by DoDI 3216.02. When applying 45 CFR 46, subpart B, actions required by any official of the Department of Health and Human Services (DHHS) shall be made by the ASD(R&E) or designee. Research involving pregnant women as subjects may be exempt from the requirements of this subpart if the research meets the exemption criteria research at section 32 CFR 219.101(b).

For purposes of applying subpart B, the phrase “biomedical knowledge” in subpart B shall be replaced with “generalizable knowledge” throughout the subpart.

Per DODI 3216.02, the additional requirements in 45 CFR 46, subpart B are applied only to research involving the following two conditions:

- a. Pregnant women as human subjects involved in research that is more than minimal risk and includes interventions or invasive procedures to the woman or the fetus;
OR,
- b. Fetus or neonate as human subjects.

Additionally, requirements at 42 USC 289g–289g-2 regarding the use of fetal tissue and transplantation of fetal tissue must be met.

11 Prisoners as Subjects

11.1 Research Intending to Include Prisoners as Subjects

Human subject research that includes prisoners must meet the additional relevant protections of 45 CFR 46, subpart C as modified by DoDI 3216.02.

Research intended to include prisoners as subjects cannot be reviewed through an expedited review procedure. The IRB reviewing prisoner research shall be composed of at least one prisoner representative, who must be present for a quorum.

11.2 Categories of Allowable Research Involving a Prisoner

In addition to the four categories of permissible human subject research identified in 45 CFR 46, subpart C, two additional categories are allowable per DoDI 3216.02:

- a. Epidemiological research that meets the following criteria:
 - (1) The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor associations for a disease.
 - (2) The research presents no more than minimal risk.
 - (3) The research presents no more than an inconvenience to the human subject.
 - (4) Prisoners are not a particular focus of the research.

- b. Human subject research that would meet the criteria described at section 32 CFR 219.101(b) can be conducted, but the research must be approved by a convened IRB and meet the requirements of subpart C and DoDI 3216.02.

11.3 When a Subject Becomes a Prisoner

When a previously enrolled subject becomes a prisoner and the research protocol was not reviewed and approved by the IRB to enroll prisoners as subjects, the investigator shall promptly notify the IRB. DoDI 3216.02 outlines the requirements for allowing the subject-now-prisoner to continue in the research and describes when the subject-now-prisoner's participation must be suspended.

12 Disclosure of Provision for Medical Expenses if Injured

All non-exempt human subject research shall, at a minimum, meet the requirement of 32 CFR 219.116(a)(6) with respect to disclosure for medical expenses, if subjects are injured. The Common Rule does not require payment or reimbursement of medical expenses, provision of medical care, or compensation for research-related injuries.

Per DoDI 3216.02, DoD Components shall establish procedures to protect human subjects from medical expenses (not otherwise provided or reimbursed) that are the direct result of participation in DoD-conducted non-exempt research involving human subjects that involves more than minimal risk. Such procedures may consist of utilizing the Secretarial Designee program as described by 32 CFR 108.4(i) during the period of the human subject's involvement in the research, which may be extended further upon the approval of the Under Secretary of Defense (Personnel & Readiness) USD(P&R). DoD Components may supplement this Secretarial Designee procedure with additional procedures consistent with applicable authority. 32 CFR 108.4(i) states that the use of regulatory authority to establish DoD health care eligibility for individuals without a specific statutory entitlement or eligibility shall be used very sparingly, and only when it serves a compelling DoD mission interest. When used, it shall be on a reimbursable basis, unless non-reimbursable care is authorized by 32 CFR 108 or reimbursement is waived by the USD(P&R) or the Secretaries of the Military Departments when they are the approving authority.

This requirement does not apply when the DoD is supporting the research but is not engaged in the non-exempt research involving human subjects (i.e., when the non-exempt research involving human subjects is performed solely by non-DoD institutions).

The DON implements this requirement via SECNAVINST 3900.39D which states "...every project involving greater than minimal risk shall include an arrangement for emergency treatment and necessary follow-up for any research-related injury. IRBs will determine whether research involving minimal risk also might include a similar arrangement for research-related injury.

References and Additional Resources

The references identified in this module are listed below in the order presented in the module.

1. References Identified in this Module

[21 CFR 50](#) – “Protection of Human Subjects,” Food and Drug Administration

[21 CFR 56](#) – “Institutional Review Boards,” Food and Drug Administration

[21 CFR 312](#) – “Investigational New Drug Application,” Food and Drug Administration

[21 CFR 600](#) – “Biological Products: General,” Food and Drug Administration

[21 CFR 812](#) – “Investigational Device Exemptions,” Food and Drug Administration

[32 CFR 108](#) – “Health Care Eligibility under the Secretarial Designee Program and Related Special Authorities”

[32 CFR 219](#) – “The Federal Policy for the Protection of Human Subjects,” DoD

[45 CFR 46](#) – “The Federal Policy for the Protection of Human Subjects,” Department of Health and Human Services

[DoDI 3216.02](#) – “Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research,” October 20, 2011

[50 USC 1520a](#) – “Restrictions on Use of Human Subjects for Testing of Chemical or Biological Agents”

[Federal Register, Volume 63, pages 60364-60367, November 9, 1998](#) – “Protection of Human Subjects: Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) Through an Expedited Review Procedure”

[Public Law 103-160, Section 252](#) – “Inclusion of Women and Minorities in Clinical Research Projects”

[42 USC 289g-289g-2](#) – “Fetal Research”

[10 USC 980](#) – “Limitations on Use of Humans as Experimental Subjects”

[SECNAVINST 3900.39D](#) – “Human Research Protection Program”

2. DoD Component-Specific Information

US Army

Army Human Research Protection Office (AHRPO)

The mission of the Army Human Research Protections Office (AHRPO) is to provide leadership in the protection of the rights, welfare, and well-being of subjects involved in research conducted or supported by the U.S. Army. AHRPO develops Army-level policy, negotiates new and oversees existing DoD Assurances, provides clarification and guidance, develops educational programs and materials, maintains regulatory oversight, and provides advice on ethical and regulatory issues in biomedical, behavioral, and social research.

Web site: <http://ahrpo.amedd.army.mil/default.cfm>

Contact: Phone: 703-882-3616 or Email: OTSG.AHRPO@amedd.army.mil

Department of the Navy (DON)

Department of the Navy Human Research Protection Program (DON HRPP)

The mission of the DON HRPP is to ensure the provision of ethical treatment of human subjects in DON research by promoting adherence to ethical principles, laws, regulations, and policies for the protection of human subjects.

For DON HRPP information, please visit:

<http://www.med.navy.mil/bumed/humanresearch/Pages/default.aspx>

Contact: human.research@med.navy.mil

US Air Force

The Air Force Research Compliance Office coordinates policy and provides guidance for human research and interprets regulations for the HRPP.

[Air Force Instruction 40-402 Protection of Human Subjects in Research](#)

Contact: afmsa.sge.c@pentagon.af.mil

Office of the Under Secretary of Defense (Personnel and Readiness) (USD(P&R))

The OUSD(P&R) includes institutions such as Department of Defense Education Activity (DoDEA), TRICARE Management Activity (TMA), Health Affairs (HA), Reserve Affairs (RA), Military Community & Family Policy (MC&FP), and Uniformed Services University of the Health Sciences (USUHS).

Find the most current data available on the USD(P&R) Human Research Protection Program by visiting:

<http://home.fhpr.osd.mil/resources/research-regulatory-oversight/hrpp.aspx>

Additional information for OUSD(P&R) supported research: OUSD(P&R) Specific and Unique Requirements

http://home.fhpr.osd.mil/Libraries/HRPP_Documents/DoD_OUSD_PR_Specific_Unique_Requirements.sflb.ashx

Contact : hrpp@tma.osd.mil

Defense Advanced Research Projects Agency (DARPA)

DARPA's instruction for handling DARPA-funded programs involving human subject research: DARPA Instruction (DI) No. 66, "Protection of Human Subjects in Research," dated January 25, 2012. Contact the email address below for a copy of the policy.

For further information on DARPA funded programs:

<http://www.darpa.mil/>

Contact: DARPAHSR@darpa.mil

Defense Threat Reduction Agency (DTRA)

DTRA Directive 3216.01, Human Subjects Protection Program and Animal Use Oversight Program, 9 June 2010

DTRA Instruction 3216.02, DTRA Implementation of the Human Subjects Protection Program and Animal Use Oversight Program, 21 Oct 2012

Please contact the email address below for a copy of the policies.

Contact: Phone: 703 767-3360 or Email: Research.Oversight@dtra.mil

National Geospatial-Intelligence Agency (NGA)

Contact Email: hrpp@nga.mil

Joint Task Force National Capital Region Medicine (JTF CapMed)

[JTF CapMed Instruction 3216.02](#), “Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research”

Web site: <http://www.capmed.mil/jtfcapmedissuances/default.aspx>

Contact: Phone: 301-319-4176 Email: charles.e.mcqueen.mil@health.mil