Department of Defense
DIRECTIVE

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SUBJECT: Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research

References: (a) DoD Directive 3216.2, "Protection of Human Subjects in DoD-Supported Research," January 7, 1983 (hereby canceled)
(b) Section 980 of title 10, United States Code
(c) Title 32, Code of Federal Regulations, Part 219, "Protection of Human Subjects," current edition
(d) DoD Directive 6200.2, "Use of Investigational New Drugs for Force Health Protection," August 1, 2000
(e) through (m), see enclosure 1

1. REISSUANCE AND PURPOSE

This Directive:

1.1. Reissues reference (a) to update policies for protecting the rights and welfare of humans as subjects of study in Department of Defense (DoD)-supported research, development, test and evaluation, and other related activities hereafter referred to as "research."

1.2. Implements 10 U.S.C. 980 (reference (b)).

1.3. Supports implementation of 32 CFR Part 219 (reference (c)), referred to as the "Common Rule."

1.4. Establishes other DoD policies for the ethical conduct of research.

2. APPLICABILITY AND SCOPE

This Directive:

2.1. Applies to the Office of the Secretary of Defense, the Military Departments, the Chairman of the Joint Chiefs of 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 in the Department of Defense (hereafter referred to collectively as "the DoD Components").

2.2. Applies to research involving human subjects, as defined herein, conducted by a DoD Component (i.e., intramural) and other research that is supported by a DoD Component (i.e., extramural) through a contract, grant, cooperative agreement, or other arrangement.

2.3. Does not apply to the use of investigational new drugs, biological products, or devices for purposes of Force Health Protection. Such use is not research and is governed by DoD Directive 6200.2 (reference (d)).

2.4. Does not apply to accepted medical practice, including the use of investigational products in such practice, undertaken for purposes of treatment, not research. Such medical practice is not research and is not subject to this Directive.

3. DEFINITIONS

Terms used in this Directive are as defined in enclosure 2.

4. POLICY

It is the policy of the Department of Defense that:

4.1. Protection of Human Subjects in Research. The rights and welfare of human subjects in research supported or conducted by the DoD Components shall be protected. This protection encompasses basic respect for persons, beneficence, and justice in the selection of subjects.

4.2. Informed Consent. In general, as required by reference (b), no DoD Component may conduct or use appropriated funds to support research involving a human being as an experimental subject without the prior informed consent of the subject.

4.2.1. In the case of research intended to be beneficial to the subject, if the subject lacks capacity, due to age, condition, or other reason, to make a decision regarding consent to participate in the research, prior consent may be provided by a legal representative of the

subject. In any such case, the determination that research is intended to be beneficial to the subject must be made by an Institutional Review Board (IRB) under reference (c).

4.2.2. Consistent with 10 U.S.C. 980(b) (reference (b)), the requirement for prior informed consent under paragraph 4.2. or subparagraph 4.2.1. may be waived by the Head of a DoD Component with respect to a specific research project to advance the development of a medical product necessary to the Armed Forces if the research project may directly benefit the subject and is carried out in accordance with all other applicable laws and regulations, including 21 CFR 50.24 (reference (j)).

4.3. Applicability of Federal Policy for Protection of Human Subjects in Research

4.3.1. The Department of Defense has joined with other Federal Agencies to adopt the "Common Rule" Federal policy for protection of human subjects in research. Reference (c) is the Department of Defense's implementation of the Common Rule. All DoD-supported and -conducted research shall comply with reference (c) and this Directive.

4.3.2. The IRBs of the DoD Components established under reference (c) shall consist of members who are either Federal employees, individuals covered under the Inter-governmental Personnel Act (IPA), or consultants consistent with the requirements established by 5 U.S.C. 3109 (reference (e)).

4.3.3. All human subject research supported or conducted by the Department of Defense shall be conducted under an assurance of compliance acceptable to the funding Agency. Research performed at DoD facilities and funded by the Department of Defense shall have a DoD assurance of compliance. The DoD Components conducting or supporting research must ensure that the investigators are familiar with the Nuremberg Code, the Belmont Report, 32 CFR Part 219 (reference (c)), this Directive, and any related requirements.

4.4. Additional Protections for Certain Categories of Research. In addition to the requirements of reference (c), the following requirements apply to research involving certain subjects or purposes.

4.4.1. Research supported or conducted by the Department of Defense that affects vulnerable classes of subjects shall meet the additional protections of 45 CFR Part 46, Subparts B, C, and D (reference (f)) (e.g., fetuses, pregnant women, human in vitro fertilization, prisoners, or children). For purposes of this paragraph, actions authorizing or requiring any action by an official of the Department of Health and Human Services (HHS) with respect to any requirements of reference (f) shall be under the authority of the Director, Defense Research and Engineering.

4.4.2. The involvement of prisoners of war as human subjects of research is prohibited.

4.4.3. For research involving more than minimal risk (as defined in 32 CFR 219.102(i), reference (c)) to subjects, an independent medical monitor shall be appointed by name. Medical monitors shall be physicians, dentists, psychologists, nurses, or other healthcare providers capable of overseeing the progress of research protocols, especially issues of individual subject/patient management and safety. Medical monitors shall be independent of the investigative team and shall possess sufficient educational and professional experience to serve as the subject/patient advocate.

4.4.3.1. Depending on the nature of the study, the medical monitor may be assigned to assess one or more of the following phases of a research project: subject recruitment, subject enrollment, data collection, or data storage and analysis.

4.4.3.2. At the discretion of the IRB, the medical monitor may be assigned to discuss research progress with the principal investigator, interview subjects, consult on individual cases, or evaluate adverse event reports. Medical monitors shall promptly report discrepancies or problems to the IRB. They shall have the authority to stop a research study in progress, remove individual subjects from a study, and take whatever steps are necessary to protect the safety and well-being of research subjects until the IRB can assess the medical monitor's report.

4.4.4. For research involving more than minimal risk and also involving military personnel, unit officers and noncommissioned officers (NCOs) shall not influence the decisions of their subordinates to participate or not to participate as research subjects. Unit officers and senior NCOs in the chain of command shall not be present at the time of research subject solicitation and consent during any research recruitment sessions in which members of units under their command are afforded the opportunity to participate as research subjects. When applicable, officers and NCOs so excluded shall be afforded the opportunity to participate as research subjects in a separate recruitment session. During recruitment briefings to a unit where a percentage of the unit is being recruited to participate as a group, an ombudsman not connected in any way with the proposed research or the unit shall be present to monitor that the voluntary nature of individual participants is adequately stressed and that the information provided about the research is adequate and accurate.

4.4.5. Research involving use of human subjects for testing of chemical or biological agents is generally prohibited by 50 U.S.C. 1520a (reference (g)), subject to possible exceptions for research for prophylactic, protective, or other peaceful purposes. Any such research shall comply with reference (g).

4.5. Education and Training on Protection of Human Subjects in Research. Awareness of human subjects protection requirements shall be established for all DoD personnel involved in the conduct, review, or approval of research covered by this Directive.

4.5.1. Awareness activities shall be commensurate with the duties and responsibilities of the participants in the process of protection of human subjects of research, and compatible with Office of Human Research Protections (OHRP) policies.

4.5.2. Research ethics training shall be incorporated into the continuing education program at all DoD Component activities that conduct research involving human subjects.

4.6. Inclusion of Women and Minorities in Clinical Research Projects. The selection of subjects reflecting gender and minority participation as appropriate shall comply with section 252 of Pub. L. 103-160 (reference (h)). The Head of the DoD Component concerned may exercise the waiver authority under this law.

4.7. Fetal Tissue Research. Fetal tissue research supported or conducted by the Department of Defense shall comply with 42 U.S.C. 289g - 289g-2 (reference (i)).

4.8. Research Misconduct. All DoD Components shall establish procedures to monitor and review the ethical conduct of research. The DoD Components that conduct or support research shall ensure that data and data collection are conducted in an ethical manner. In cases in which data are not collected in an appropriate manner, the DoD Component shall determine if the misconduct was intentional or reckless; was an isolated event or part of a pattern; had significant impact on the research record; or had significant impact on other researchers or institutions. The DoD Component shall initiate and carry through on any actions that are necessary to ensure resolution of misconduct findings. All findings of serious research misconduct under this section shall be reported to the Director, Defense Research and Engineering.

4.9. Relationship to Other Requirements. Some activities subject to this Directive may also be subject to regulations of other Federal Agencies, organizations, and non-U.S. entities. Examples include: Food and Drug Administration policies regarding investigational drugs, vaccines, biological products, or devices; multi-agency research; and international research. Activities subject to this Directive and one or more of these other requirements shall comply with all applicable requirements (e.g., references (c) (32 CFR 219.101(g) and (h)), (j), (k), and (l)).

4.10. Non-compliance. Issues related to non-compliance with this Directive by any DoD Component, subordinate, or supported activity shall be referred initially to the next higher management echelon to take deliberate action to resolve. All findings of serious non-compliance under this section shall be reported to the Director, Defense Research and Engineering.

5. RESPONSIBILITIES

5.1. The Director, Defense Research and Engineering, under the Under Secretary of Defense *for* Acquisition, Technology, and Logistics:

5.1.1. Shall be the single point of contact within the Department of Defense for all matters relating to the Department of Defense's compliance with the "Common Rule" and act as the principal DoD liaison with Agencies outside the Department of Defense on matters pertaining to protection of human subjects in research.

5.1.2. May initiate updates to reference (c) and issue any DoD Instructions or other guidance necessary to implement this Directive. With respect to matters affecting medical research, this shall be done in coordination with the Assistant Secretary of Defense (Health Affairs) (ASD(HA)).

5.1.3. Shall establish a committee to coordinate DoD Component activities in the protection of human subjects. The committee shall be composed of representatives from the DoD Components' human subject protection offices.

5.1.4. Shall exercise the authorities of the Secretary of Defense under reference (c), except for matters not delegable, reserved, or covered by another specific delegation.

5.1.5. Shall establish procedures and standards, consistent with the Federal Policy on Research Misconduct (reference (m)), for the prevention of research misconduct in the Department of Defense.

5.1.6. May grant exceptions to policy under this Directive if justified by special circumstances and consistent with law. Records shall be maintained on exceptions granted under this Directive.

5.2. The Assistant Secretary of Defense for Health Affairs, under the Under Secretary of Defense for Personnel and Readiness shall:

5.2.1. Advise the Director, Defense Research and Engineering on matters related to the involvement of human subjects in research, especially, regarding medical safety, ethics, and standards of professional care and conduct.

5.2.2. Serve as the DoD representative on matters relating to implementation of Food and Drug Administration regulatory requirements (references (j) and (k)).

5.3. The Heads of the DoD Components shall:

5.3.1. Develop, issue, and monitor implementing policies to ensure compliance with this Directive and with any implementing Instructions issued under the authority of this Directive. In research undertakings in which more than one DoD Component is involved, the Heads of the Components shall determine and jointly assign executive responsibility for compliance.

5.3.2. Maintain adequate documentation of DoD-supported or -conducted research involving human subjects and establish procedures for supporting DoD reporting requirements.

5.3.3. Delegate authorities and responsibilities under this Directive to levels of command or authority appropriate to ensure compliance. This shall include procedures for the investigation and resolution of allegations of non-compliance, and may include procedures for headquarters-level administrative review of research. A DoD Component may delegate

headquarters-level research review responsibility to another DoD Component for purposes of efficiency and consolidation of functional offices.

5.3.4. With respect to research for which primary involvement is from the Department of Defense, establish the required administrative procedures to protect human subjects from medical expenses (not otherwise provided or reimbursed) that are the direct result of participation in a research project involving more than minimal risk. For this purpose the determination of primary involvement shall be based on consideration of the DoD portion of the total involvement (i.e., funding, personnel, facilities, and all other resources) in the research.

6. EFFECTIVE DATE

This Directive is effective immediately.

Paul Wolfowitz
Deputy Secretary of Defense

Enclosures - 2
E1. References, continued
E2. Definitions

E1. ENCLOSURE 1

REFERENCES, continued

(e) Section 3109 of title 5, United States Code, "Employment of Experts and Consultants, Temporary or Intermittent"
(f) Title 45, Code of Federal Regulations, Part 46, "Protection of Human Subjects," Subparts B, C, and D
(g) Section 1520a of title 50, Unites States Code, "War and National Defense"
(h) Section 2358 note of title 10, United States Code, "National Defense Authorization Act for Fiscal Year 1994," (Public Law 103-160, Sec. 252)
(i) Sections 289g - 289g-2 of title 42, United States Code, "Public Health and Welfare"
(j) Title 21, Code of Federal Regulations, Subchapters A, D, F, and H, "Food and Drug Administration"
(k) Memorandum of Understanding between the Food and Drug Administration and the Department of Defense, "Concerning Investigational Use of Drugs, Antibiotics, Biologicals, and Medical Devices by the Department of Defense," May 1, 1987
(l) DoD Directive 6000.8, "Funding and Administration of Clinical Investigation Program," November 3, 1999
(m) Federal Policy on Research Misconduct, Office of Science and Technology Policy, 65 Federal Register 76260-76264 (December 6, 2000)

E2. ENCLOSURE 2

DEFINITIONS

E2.1.1. Common Rule. The regulation adopted by multiple Federal Agencies for the protection of human subjects in research. The Department of Defense's implementation of the Common Rule is at 32 CFR 219, "Protection of Human Subjects" (reference (c)).

E2.1.2. Research. Any systematic investigation, including research, development, testing, and evaluation (RDT&E), designed to develop or contribute to generalizable knowledge.

E2.1.3. Research Involving a Human Being as an Experimental Subject. 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 (32 CFR 219.102(f), reference (c)). Examples of interventions or interactions include, but are not limited to, a physical procedure, a drug, a manipulation of the subject or subject's environment, the withholding of an intervention that would have been undertaken if not for the research purpose. This does not include:

E2.1.3.1. Activities carried out for purposes of diagnosis, treatment, or prevention of injury and disease in members of the Armed Forces and other mission essential personnel under Force Health Protection programs of the Department of Defense.

E2.1.3.2. Authorized health and medical activities as part of the reasonable practice of medicine or other health professions.

E2.1.3.3. Monitoring for compliance of individuals and organizations with requirements applicable to military, civilian, or contractor personnel or to organizational units. This includes such activities as drug testing, occupational health and safety monitoring, and security clearance reviews.

E2.1.3.4. Activities exempt under 32 CFR Part 219 (reference (c)).

E2.1.4. Support. Unless otherwise clarified in a specific paragraph of this Directive, this term generally means the provision of funding, personnel, facilities, and all other resources.