# Research Involving Department of Defense Funding

## Purpose

The policy provides guidance to Boston Children's Hospital (BCH) researchers whose human subjects research involves any component of the Department of Defense (DoD) funding or support.

## Policy

### Scope and Applicability

This information and guidance apply to all human subjects research involving the DoD. Research is considered to involve the Department of Defense when:

A. The research is funded by a component of DoD.

B. The research involves cooperation, collaboration, or other type of agreement with any component of DoD.

C. The research uses property, facilities, or assets of a component of DoD.

D. The subject population will intentionally include personnel (military ancd/or civilian) from a component of DoD.

Boston Children's Hospital does not conduct research that intentionally involves military personnel.

*DoD policies and requirements do not apply when DoD personnel incidentally participate as subjects in research that is not supported by DoD, and DoD personnel are not an intended population of the research*.

IRB administrative staff, IRB Chairs and IRB members are made aware that a protocol is funded by the Department of Defense by reviewing the funding agency listed on the research protocol.

This policy and the associated additional review requirements are made available on the IRB website, and the IRB reviewer worksheets link to the associated policy and its requirements. The IRB Administrative Director will also advise IRB reviewers as necessary during the review process.

### Background

In the past few years, DoD has significantly enhanced their human subjects protection requirements, including the application of those requirements to researchers who are not employees of the DoD. From time-to-time, BCH investigators will receive funds from DoD and therefore the additional regulations will apply.

Example A (above) describes the type of DoD research that is most frequently conducted at BCH to date. Examples B-D are much less common.

As necessary and requested by DoD, Boston Children's Hospital will sign an Addendum to its Federalwide Assurance (FWA). This document requires that BCH apply DoD regulations and policies for the protection of human research subjects when conducting, reviewing, approving, overseeing, supporting or managing human subjects research involving the DoD. DoD directive 3216.2 provides the hospital with the additional DoD requirements.

Principal investigators (PIs) will need to include in their protocol the additional information required so that the IRB may take them into consideration to make the DoD requirements and determinations.

DoD will require documentation of Institutional Review Board (IRB) approval, the risk level, and the expiration date of the research to the DoD component sponsoring or supporting the study.

The DoD may also request additional documentation to verify compliance with federal and DoD policies, including minutes related to the research, any exemption determinations, or documentation of continuing approval.

The DoD applies the provisions in 45 CFR Part 46, Subparts B, C, and D for the protection of vulnerable classes of subjects but prohibits the use of prisoners of war in DoD sponsored research.

Research that involves greater than minimal risk requires appointment of an independent research monitor. In certain cases, the DoD also applies limitations on the waiver of informed consent.

Civilian researchers attempting to access military volunteers should seek collaboration with a military researcher familiar with service-specific requirements.

## Definitions

**Research Involving a Human Being as an Experimental Subject** is defined 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 [32 CFR 219.102(f), reference (c)]. Examples 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.

The following activities are **not considered research** involving human participants:

- Public or internal information collections of facts or opinions, obtained initially or in follow-up requests, from individuals (including individuals in control groups) under treatment or clinical examination in connection with research on, or prophylaxis to prevent, a clinical disorder;
- Direct treatment of that disorder; or
- The interpretation of biological analyses of body fluids, tissues, or other specimens; or the identification or classification of such specimens.

**DoD Components** refers collectively to the organizational entities within the DoD that are subject to the human subjects protections laid out in Department of Defense Directive.

**Research Monitor** refers to a physician, dentist, psychologist, nurse, or other healthcare provider designated to oversee a specific protocol that involves more than minimal risk, especially issues of individual subject/patient management and safety. The research monitor functions independently of the research team and shall possess sufficient educational and professional experience to serve as the subject/patient advocate.

**Minimal Risk:** The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests**.**

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.)

## Procedure

### 1. Scientific Review:

a. New Research: DoD requires scientific review prior to IRB review for all new DoD supported human research. The IRB policy: ***Department/Division Scientific Review of Human Subjects Research*** requires departmental scientific review prior to IRB submission, thus meeting this requirement.

b. Amendments: DoD also requires that all substantive amendments to approved DoD research involving human subjects receive scientific review prior to IRB review. Substantial amendments must be submitted for departmental review prior to submission to the IRB, for guidance concerning changes that do not qualify as minor see the IRB policy: ***Revisions and Amendments***. Amendments that are submitted to the full IRB constitute substantial amendments.

### 2. Education Requirements

DOD requires initial and continuing mandatory education requirements for human subjects protections. Boston Children's Hospital requirements for mandatory and continuing education meet this requirement.

- The DoD component may evaluate the education policies to ensure the personnel are qualified to perform the research, based on the complexity and risk of the research.

See IRB policy: ***Education and Training: Investigators and Research Staff.***

### 3. Research Monitor Required: Greater than Minimal Risk Studies

For DoD-sponsored research involving greater than minimal risk to subjects, the DOD requires appointment of an independent research monitor. The research monitor has the authority to:

a. Stop a research study in progress;
b. Remove individuals from the study;

c. Take any steps to protect the safety and well–being of subjects until the IRB can assess the research monitor's report.

The PI in coordination with the IRB identifies a candidate for the position of research monitor, taking into account the nature and disciplinary focus of the study and the likely type of medical expertise required. The IRB also ensures that the research monitor is independent of the research team.

## 4. Research Involving International Citizen Populations

For research conducted internationally the IRB policy for international research: ***International Research/Cross Cultural Research*** will meet the DOD requirements.

This includes taking into consideration subject populations, the cultural context, the languages understood by the human subjects, identifying and considering local laws, regulations, customs and practices. In addition, determinations are made as to whether the sponsoring DoD Component requires an additional ethics review by the host country or a local DoD IRB with host country representation. Boston Children's Hospital or the investigator will also require permission to conduct research in that country by certification or local ethics review.

## 5. Limitations on Waiver of Consent and Exception from Informed Consent in Emergency Medicine

DoD imposes limitations on waiver of consent for human subject research.

The IRB may only waive the consent process if the research being considered does not meet the definition of 'research involving a human being as an experimental subject."

DoD regulations also prohibit an exception from informed consent in emergency medicine research. These requirements limiting the ability to waive consent may be waived by the Secretary of Defense under certain circumstances.

## 6. Informed Consent from Legal Representatives of Adult Subjects Who Cannot Consent

When research meets the definition of research involving a human being as an experimental subject, and consent is to be obtained from the experimental subject's legal representative, the research must intend to benefit the individual subject. The determination that research is intended to be beneficial to the individual experimental subject must be made by an IRB.

## 7. Multi-Site or Collaborative Research Requirements

Any investigator developing a proposal for DoD funding or other support that involves other collaborating institutions needs to consult the sponsoring DoD Component and ORI staff to identify additional requirements for multi-site research. Formal agreements may be necessary to ensure that participating institutions understand and accept their scope of work specific roles and responsibilities of each party are agreed upon. The BCH policies for reliance agreements could be considered for DOD funded research.

## 8. Provisions for Research-related Injury

The PI is responsible for informing the IRB if there are any requirements from DoD Component's provision of care in the case of a research-related injury. If the DoD Component has stricter requirements than the Common Rule or BCH policies, this will need to be discussed and agreed upon by General Counsel and the VP of Research Administration.

These requirements will also need to be disclosed in the informed consent document.

## 9. Research Involving U.S. Military Personnel as Research Participants

If any research includes U.S. military personnel as subjects, the IRB protocol must include a plan for research subject recruitment that incorporates additional safeguards to minimize undue influence or coercion from individuals within a potential subject's chain of command. The PI is required to consult with the sponsoring DoD Component to determine appropriate recruitment plans. In addition, unless on leave status during research participation, military personnel may not receive compensation for their participation

## 10. Prisoners of War

Under No circumstances shall the IRB approve research involving prisoners of war, as defined by the specific DoD Component.

## 11. Additional DoD Review Required Prior to Initiation of Study

After the IRB completes its review and issues approval, the PI through the Office of Sponsored programs will need to submit to the DoD Component sponsoring or supporting the study documentation of: the IRB approval, the risk level, and the expiration date of the research to the. The DoD may also request additional documentation to verify compliance with federal and DoD policies, including minutes related to the research.

The PI may not initiate the study until the human research protection officer within the sponsoring DoD Component reviews and approves the IRB approval and other submitted documentation.

If the study is for DoD-sponsored survey research or survey research within the DoD that involves DoD personnel, including military personnel, an additional level of DoD review of the study may be required. Surveys typically require DoD Survey Review and approval. The PI submits surveys and all required documentation relevant to survey research review to the requesting DoD Component.

## 12. The following shall promptly (no longer than within 30 days) be reported to the DoD human research protection officer:

a. When the Organization is notified by any Federal department, agency or national Organization that any part of the HRPP is under investigation for cause involving a DoD-supported research protocol.
b. When significant changes to the research protocol are approved by the IRB.
c. The results of the IRB continuing review.
d. Change of reviewing IRB.

## 13. Unanticipated problems

Any unanticipated problems involving risks to participants or others for any DoD-supported research must be promptly (**no longer than within five days**) reported to the DoD Office for Human Research Protections

## 14. Suspension or Termination

Any suspension or termination of DoD-supported research must be promptly (**no longer than within five days**) reported to the DoD Office for Human Research Protections.

## 15. Audits, reviews, and assessments

The following must be reported to DOD HRPP **within 5 days of completion** of the report

a. Reports of for-cause audits, reviews, or assessments conducted by or on behalf of the component office of human protections.
b. Reports of audits of DoD-conducted or DoD-supported human participant research by another federal or state agency, official governing body of a Native American or Alaskan native tribe, other official entity, or foreign government, within five business days of discovering that such audit reports exist.
    - Allegations of serious or continuing noncompliance related to HSR that are substantiated by investigation, and subsequent actions taken based on the findings.
    - Substantiated allegations related to classified HSR must be reported immediately (**less than five days**) to the DOHRP.

## 16. Research involving pregnant women, prisoners, and children are subject to the DHHS Subparts B, C and D, except where modified by DODI 3216.02.:

- For purposes of applying Subpart B, the phrase “biomedical knowledge” shall be 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 included interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as participants.
- Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.
    - 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 a 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.
- 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.

## 17. In addition to allowable categories of under Subpart C, two additional categories are allowable when:

- 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 studies potential risk factor association for a disease.
  - The research presents no more than minimal risk.
  - The research presents no more than an inconvenience to the prisoner-participant.
  - Prisoners are not a particular focus of the research.
- Human participant research involving prisoners that would otherwise meet exemption criteria may be conducted, but must first be approved by an IRB.

## 18. Prisoners

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

When the IRB reviews research involving prisoners, at least one prisoner representative must be present for quorum

Research involving prisoners cannot be reviewed by the expedited procedure.

## 19. When a previously enrolled human subject becomes a prisoner and the relevant research protocol was not reviewed and approved by the IRB to include prisoners:

The Principal Investigator must promptly notify the IRB.

- For DoD-conducted research, the human protections director must notify the component office of human research protections.
- For DoD-supported research, the non-DoD organization must notify the DoD human research protection official and other federal agencies.

DoD organizations must demonstrate to the senior designated official that the IRB has fulfilled its duties in accordance with DHHS Subpart D, 45 CFR 46. 407 and 21 CFR 50.54.

If the researcher asserts to the IRB that it is in the best interest of the prisoner-participant to continue to participate in the research while a prisoner, the IRB Chair may determine that the prisoner-participant continue to participate until the convened IRB can review this request to approve a change in the research protocol and until the Organizational Official and DoD Component Office review the IRB's approval to change the research protocol. Otherwise, the IRB chair shall require that all research interactions and interventions with the prisoner-participant (including obtaining identifiable private information) cease until the convened IRB can review the request to approve a change in the research protocol.

The convened IRB, upon receipt of notification that a previously enrolled human participant has become a prisoner, shall promptly re-review the research protocol to ensure that the rights and wellbeing of the human subject, now a prisoner, are not in jeopardy.

- The IRB should consult with a subject matter expert having the expertise of a prisoner representative if the IRB reviewing the research protocol does not have a prisoner representative.
- If the prisoner-participant can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner-participant's confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research involving human participants from continuing as approved, the convened IRB may approve a change in the study to allow this prisoner-participant to continue to participate in the research.
- This approval is limited to the individual prisoner-participant and does not allow recruitment of prisoners as participants.

## 20. Research involving a detainee as a human participant is prohibited.

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.

The IRB is aware of the definition of "prisoner of war" for the DoD component granting the addendum.

## 21. Research involving the testing of chemical or biological agents is prohibited pursuant to Section 1520a of Title 50, United States Code (U.S.C.)

Some exceptions for research for prophylactic, protective, or other peaceful purposes apply. Before any excepted testing of chemical or biological agents involving HSR can begin, explicit written approval must be obtained from the DoD Office for Human Research Protections (DOHRP).

## 22. Record Maintenance

Records maintained that document compliance or noncompliance with DoD requirements and shall be made accessible for inspection and copying by representatives of the DoD at

reasonable times and in a reasonable manner as determined by the supporting DoD component.

## Related Content

IRB Policies

*Department/Division Scientific Review of Human Subjects Research*

*Education and Training: Investigators and Research Staff.*

*International and Cross-cultural Research*

*Revisions and Amendments*

Regulatory Citations

*32 CFR 219, "Protection of Human Subjects"*

*Department of Defense (DoD) Directive 3216.2, "Protection of Human Subjects and Adherence to Ethical Standards in DoD Supported Research*

## Document Attributes

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