Research sponsored by the Department of Defense (DoD) involving collaboration with DoD, or involving DoD facilities or personnel (military or civilian), is subject to additional special requirements to enhance the protection of human subjects. These requirements include special protections for research participants as well as additional review and reporting requirements for the investigator and IRB. Investigators must be aware of these special requirements when planning a research project as they may add a significant amount of time to the human subjects review and approval process throughout the research.

The focus of this guidance document is on the general requirements outlined in DoD Instruction 3216.02, Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research, November 8, 2011, and in Navy guidance SECNAV Instruction 3900.39D, Human Research Protection Program, November 6, 2006. Each DoD Component may have additional requirements beyond those included in this guidance document. PIs are advised to check with their program manager with the sponsoring Component about any additional requirements.

1. Definition of Department of Defense Research

Research is considered to involve the Department of Defense when:

- The research is funded by a DoD Component*, including cases where LLUH 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 as research subjects where they are not the intended research population or where the project is not DoD-supported).

*DoD Components include, but are not limited to:

- Air Force
- Air Force Academy
- Army
- Army Corps of Engineers
- Coast Guard
- Coast Guard Academy
- Defense Advanced Research Projects Agency (DARPA)
- Defense Intelligence Agency
- Marines
- Military Academy (West Point)
- Missile Defense Agency
- National Geospatial-Intelligence Agency
- National Guard
- National Security Agency
- National War College

- Naval Academy
- Navy
- Office of Naval Research
- Pentagon Force Protection Agency
- Tricare Health System
- U.S. Naval Observatory

2. Required DoD Human Research Protections Office (HRPO) Administrative Review

Upon completion of LLUH IRB review and approval, including determination of exempt or not IRB-regulated status, the HRPO for the sponsoring Component must perform an administrative review of the research before activities with human subjects may begin. The review involves confirmation that the University and the proposed research are in compliance with DoD requirements for the protection of human subjects.

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 the information required by the sponsoring Component.

3. Special Requirements for IRB Review of DoD Research

3.1 Training Requirements

DoD requires that all individuals involved in the "design, conduct, or approval of human subject research" complete human subject research training. LLUH Human Subjects Education training meets the training requirements for many DoD Components. Investigators are responsible for ensuring that all study team members engaged in the conduct of human subject research complete required training. The DoD Component may evaluate the institution's training program to ensure that personnel are qualified to perform the research, based upon the complexity and risk of the research.

Component specific training:

- Department of Navy (DON) (including Marine Corps)
  Principal investigators for projects sponsored by or involving DON Components must complete additional training offered by CITI (www.citiprogram.org), specifically the CITI Training Module for DON-Supported Extramural Performers. Contact Research Education for assistance with accessing this special training. This CITI training is also required for institutional and IRB leadership. The training requirement for other study staff engaged in DON research is fulfilled by completing other Human Subjects Education requirements.
- Secretary of Defense (Personnel and Readiness)
  All investigators and research staff on projects sponsored by the Secretary of Defense (Personnel and Readiness) are required to complete annual Human Subjects Education training.

3.2 Scientific Review

Research involving Components of the Army or Navy (including Marine Corps) may require documentation of scientific review prior to IRB review of new applications and substantive amendments.

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 researcher'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. Check with IRB or the DoD program manager regarding the requirement.

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;
- Facilities and resources available;

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

3.3 DoD Approval of Surveys/Interviews

Research involving surveys or interviews with DoD personnel (military or civilian) or their families must be submitted, reviewed, and approved by the DoD after the research protocol is reviewed and approved by the IRB. Check with your DoD Component regarding any additional review requirements and the timing of the review and provide documentation of this review to the IRB.

3.4 International Research

In its review of the research conducted outside of the United States, the IRB must consider the laws and requirements of the host country as well as the cultural context of the research. This is typically documented via an in-country or IRB/ethics review and/or a review by a consultant with expertise in that country.

For Navy-sponsored research that involves subjects who are not US citizens or DoD personnel, the investigator must provide the following documentation:

- Permission of the host country; and
- Ethics review and approval by the host country, or the local Naval IRB with host country representation.

3.5 Collaboration with other Institutions

Collaborating institutions in multi-site research must hold a federal-wide assurance. Investigators must provide the following:

- Documentation of IRB approval or IRB Authorization Agreement for engaged collaborators;
- Statement of compliance with special DoD requirements

4. Unique Human Subject Protections Required for DoD-related Research

4.1 Prohibited Research

- Research with detainees (prisoners of war), except research with investigational new drugs or devices 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"

- LLUH does not conduct classified research.
- Human testing of chemical or biological agents, except for certain prophylactic, protective or peaceful purposes.

4.2 Definition of "Experimental Subjects"

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."

4.3 DoD Limitations on Waivers of Informed Consent and Consent by LARs

The requirement to obtain consent cannot be waived for any research using DoD funds and meeting the definition of research involving a human being as an experimental subject (10 USC 980). This places limitations on research involving deception, decisionally-impaired individuals, or research being conducted under emergency conditions where the subject may not be able to provide consent.

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 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 in order to advance the development of a medical product necessary to the Armed Forces, but only if the research may directly benefit the subject and the research is carried out in accord with all other applicable laws and regulations.

Informed consent may be provided by a legally authorized representative (LAR) only if: (1) the subject lacks decision-making capacity; AND (2) the IRB has determined that the research is intended to be beneficial to the individual subjects.

4.4 Definition of Minimal Risk

The DoD Instruction cautions that the Common Rule definition of minimal risk that includes the phrase "ordinarily encountered in daily life or during the performance of routine physical or psychological tests" must not be interpreted to include the inherent risks that certain individuals face in their everyday lives, such as a soldier in a combat zone or an individual who has a particular medical condition.

4.5 Research Monitor for More than Minimal Risk Research

A research monitor must be appointed for all research that involves more than minimal risk. The monitor may be either a medical or non-medical monitor depending on the

nature of the research. The monitor must be independent of the research team and possess sufficient expertise to evaluate the risks and conduct of the research. The investigator must identify a research monitor by name and have the selection approved by the reviewing IRB. The IRB may choose to appoint more than one monitor for a project and may choose to appoint a monitor for research that is deemed to be no more than minimal risk. The monitor may be an ombudsman or a member of the data safety monitoring board.

The duties of the research monitor shall be determined on the basis of specific risks or concerns about the research. The research monitor may perform oversight functions (e.g., observe recruitment, enrollment procedures, and the consent process for individuals, groups or units, oversee study interventions and interactions, review monitoring plans and unanticipated problems involving risks to participants or others, and oversee data matching, data collection, and analysis). The research monitor may discuss the research protocol with the investigators, interview human subjects, and consult with others outside of the study about the research. The monitor reports observations and findings to the IRB or a designated official. The monitor has the authority to stop a research protocol in progress, remove participants from the study, or take necessary steps to protect the safety and well-being of participants until the IRB can assess the study.

The IRB must approve a written summary of the monitors' duties, authorities, and responsibilities. The IRB or HRPP official shall communicate with research monitors to confirm their duties, authorities, and responsibilities.

The Institutional Official of the DoD Component may waive the requirement for the monitor.

4.6 Vulnerable Populations

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. See DoD Instruction 3216.02, Part 7, for a description of additional DoD considerations for these populations. 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. Section 5 below describes protections for military personnel as research subjects.

4.7 DoD Protections from Medical Expenses if Injured

For more than minimal risk research, the informed consent document must provide information regarding payment of medical expenses, provision of medical care, or compensation for research- related injuries, consistent with the requirements of the Common Rule.

5. DoD Personnel as Research Subjects

5.1 Military Participants

- All active duty service members and reserve Component members are considered to be adults for the purpose of participating in DoD-conducted or supported research.
- Command approval may be required for military personnel to participate in human subject research as some types of research could impact a soldier's readiness in the

field. Investigators may be asked to provide documentation of Command approval as part of the IRB review.

- When research involves U.S. military personnel, superiors of service members (e.g., unit officers, senior noncommissioned officers, and equivalent civilians):
  - Are not permitted to influence the decision of their subordinates
  - May not be present at the time of recruitment
  - Have a separate opportunity to participate
  - When recruitment involves a percentage of a unit, an independent ombudsman must be present.
- When research involves U.S. military personnel, limitations on dual compensation:
  - Prohibit an individual from receiving pay of compensation for research during duty hours.
  - U.S. military personnel may be compensated for research if the participant is involved in the research when not on duty.
  - Non-Federal persons may be compensated for research participation other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.

5.2 DoD Civilian Personnel

DoD civilian personnel that are recruited into research are afforded the same protections as military personnel (5.1 above). The requirement for an ombudsman is at the discretion of the IRB.

5.3 Limitations on Compensation

On-duty federal personnel including military members:

- Up to $50 for blood draws;
- Compensation is not allowed for general research participation.

Off-duty federal personnel including military members:

- Up to $50 for blood draws;
- Compensation is allowed for general research participation, as approved by the IRB. Payment many not come directly from a federal source. Payment from a federal contractor or non-federal source is permissible.

Non-federal personnel:

- Up to $50 for blood draws;
- Compensation is allowed for general research participation, as approved by the IRB. Payment may come from a federal or non-federal source.

6. Other DoD-Specific Requirements

6.1 Reporting Requirements

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

- Determinations of serious or continuing noncompliance;
- Unanticipated problems involving risks to subjects or others;
- Study suspensions or terminations;
- Audits, inspections or investigators of DoD research;
- Results of Continuing Review;

- Changes to the reviewing IRB;
- Substantive amendments to the protocol. Amendments must be reviewed and approved by the HRPO prior to implementing the change to the study.

6.2 Record keeping

Consistent with LLUH 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 LLUH.

For further information

DoD Regulations and Guidance: 32 CFR 219, Protection of Human Subjects; DoD Instruction 3216.02, Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research, November 8, 2011; 10 USC 980, Limitations on the Use of Humans as Experimental Subjects Department of Defense Directive 3210.7, Research Integrity and Misconduct; Department of Defense Directive 6200.2, Use of Investigational New Drugs in Force Health Protection

Department of Defense, Office of the Secretary of Defense for Personnel and Readiness: HA Policy 05.003, Policy for Protection of Human Subjects in Department of Defense Sponsored Research

Department of the Army: AR 70-25, Use of Volunteers as Subjects of Research, January 25, 1990 AR 40-38, Clinical Investigation Program, September 1, 1989; AR 40-7, Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances, October 19, 2009

Department of the Navy: SECNAV Instruction 3900.39D, Human Research Protection Program, November 6, 2006 Department of the Navy, Training and Education Guidance

Department of the Air Force: Air Force Instruction 40---402, Protection of Human Subjects in Research