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Approved By: ORI Director	Signature	Date	Date First Effective: 11-10-09
Approved By: Nonmedical IRB Chair	Signature	Date	
Approved By: Medical IRB Chair	Signature	Date	Revision Date: 03-29-12

OBJECTIVE

To describe policies and procedures at the University of Kentucky (UK) for institutional review and oversight of research supported by the Department of Defense (DoD) that involves human subjects

GENERAL DESCRIPTION

Human research supported by the DoD is subject to the Federal Policy for the protection of human subjects in research, i.e., the Common Rule. However, because of the DoD culture, organizational structure, and population, DoD Directive 3216.02 lays out additional requirements that apply as well. These requirements are designed to cover risks unique to DoD personnel that differ from civilians both in the conduct of research and in participation in research (e.g., deployability, personal conduct standards, and duty to report certain personnel actions). The procedures outlined in this SOP ensure that UK research supported by the DoD complies with DoD regulations governing human research.

UK's existing Federalwide Assurance (FWA) of compliance approved by the Office of Human Research Protections (OHRP) meets the DoD requirement that the institution hold a federal assurance. The existing FWA may, however, be augmented with a DoD Addendum to inform institutions of additional DoD requirements.

The principal investigator (PI), with assistance from ORI, submits 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, determinations that an activity is not human research, any exemption determinations, or documentation of continuing approval.

The DoD applies the provisions in 45 CFR 46, Subparts B, C, and D with modifications for the protection of vulnerable classes of subjects. Additionally, DoD has limitations on the involvement of detainees in DoD supported research. Additional safeguards apply when the

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study involves DoD personnel (both military and civilian) or international citizen populations as subjects. UK does not apply DoD policies when U.S. military DoD personnel incidentally participate as subjects in a study that is not DoD-sponsored or supported **and** DoD personnel are not the intended target population.

Research involving greater than minimal risk [as defined in 32 CFR 219.102(i), reference (c)] requires appointment of an independent research monitor.

The subset of research involving human beings as Experimental Subjects includes limitations on the waiver of informed consent.

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)]. Research involving a human being as an experimental subject is a subset of research involving human subjects. This definition does not include activities that are not considered research involving human subjects, activities that meet exemption criteria, and research involving the collection or study of existing data, documents, records, or specimens from living individuals. 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 term *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 3216.02. These entities include 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 within the DoD.

Support of a study generally means the provision of at least a portion of the funding, personnel, facilities, and all other resources. Under this definition, studies that may be wholly funded internally or by a non-DoD component, such as an agency within the Department of Health and Human Services, but focus, for example, on a health concern prevalent in military populations may still fall under DoD purview. Such studies may, for example, require the commitment of DoD personnel as subjects, access to or information about DoD personnel for recruitment, identifiable data or specimens from living individuals, or the use of other DoD data resources.

A *DoD Addendum* to the institution's existing FWA is one of several methods that can be used to inform institutions (Institutional Officials and IRB chairs) of DoD research requirements that differ from the OHRP-approved FWA. The DoD Addendum may include designation of the relied-upon IRB(s) and/or an outline of requirements specific to a given DoD Component. The DoD Addendum is effective as long as the FWA is in force.

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Research Monitor refers to an individual 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 expertise consistent with the nature of risk(s) identified within the research protocol, in order to protect the safety and well-being of human subjects.

Detainee is defined as any person captured, detained, held or otherwise under the control of DoD personnel (military, civilian, or contractor employee). It does not include persons being held primarily for law enforcement purposes, except where the United States is the occupying power.

DoD Personnel includes DoD civilian employees and members of the military services, unit officers, and noncommissioned officers (NCOs).

RESPONSIBILITY

Execution of SOP: PI/Study Personnel, Vice President for Research (VPR), IRB, IRB Chair, Office of Research Integrity (ORI) Director, ORI Staff, Office of Sponsored Projects Administration (OSPA) Staff

PROCEDURES

Department of Defense Addendum to the Existing FWA

1. After a PI submits an application to a DoD component, OSPA may receive notice from the DoD that a DoD Addendum to the existing FWA may facilitate the sponsored research agreement for a pending award. OSPA staff notify the PI and the ORI of the DoD request.
2. The ORI Director or designee reviews the requirements of the DoD Addendum and designates select UK IRB(s) to review and oversee DoD-sponsored research.
3. The Institutional Official (VPR), the appropriate IRB Chair, and the ORI Director review and sign the DoD Addendum.
4. Once a DoD Addendum is in place, it covers all UK DoD-sponsored research for that Component; however, various DoD Components may use other processes or have additional requirements. The PI, with assistance from ORI, is responsible for identifying additional requirements and conveying those requirements to the IRB, as appropriate.

Exempt Human Subject Research

When human subject research meets the criteria for exemption at 45 CFR 46.101(b), the PI follows standard procedures in accord with the Exempt Review SOP. The PI sends a copy of the IRB Exemption Approval letter with the justification to the DoD for review and concurrence.

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Expedited Human Subject Research

1. The IRB uses expedited review procedures to review minimal risk, non-exempt research involving human subjects using materials (e.g., data, documents, records, or specimens) that have previously been collected for any purpose, provided the materials were not collected for the currently proposed research.

Submission of DoD Supported Research to the IRB

1. DoD requires a scientific review of the protocol. The PI is responsible for obtaining a comprehensive scientific review from his/her Department Chair or designee prior to submission of the application to the IRB. The Department Chair or designee is responsible for conducting the scientific review and signing off on the IRB application. The IRB considers the scientific merit of the study relative to human subject protection.
2. The PI or designee completes an application for IRB review of the protocol and makes the initial determination identifying the research as *supported* by a DoD component (as defined in Department of Defense Directive 3216.02) and submits it to the ORI.
3. The PI is responsible for checking the appropriate DoD-relevant items on the IRB application. If the study involves a DoD Component, the PI adds “UK/D:” at the beginning of the study title. The PI indicates in the application whether DoD personnel or international citizen populations are subjects.
4. Upon receipt of the application, ORI staff screen it for completeness and accuracy consistent with the Initial Review SOP and make a preliminary determination that the research is DoD-supported. ORI staff also make preliminary determinations of the level of risk, the type of review, the type of subjects involved (i.e., DoD personnel or international citizen populations), potential need for an ad hoc or cultural consultant, and the need for a research monitor (see *Research Monitor* below).
5. ORI staff advise the PI and the IRB of DoD-specific requirements in the Addendum. The PI is responsible for communicating with the DoD to identify DoD component requirements specified in the grant application guidelines and advising the ORI staff and IRB of the requirements.
6. The PI and study personnel are responsible for completing processes specified in the DOD Addendum or DOD guidelines and submitting documentation, as appropriate, to the ORI as an attachment to the IRB application.

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Department of Defense Ethics Education Requirements

1. The PI and research team complete all initial and continuing mandatory education requirements for human subjects protections in accordance with UK policy (See University of Kentucky Mandatory Research Education Requirements).
2. The PI, with assistance from ORI staff, is responsible for identifying specific educational or certification requirements of the sponsoring DoD Component and conveying those requirements to the IRB. The PI consults the DoD Component, as appropriate, to identify education requirements

Research Monitor Required: Greater than Minimal Risk Studies

1. 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:
 - Stop a research study in progress;
 - Observe subject recruitment when conducted in a group setting;
 - Remove individuals from the study; and
 - Take any steps to protect the safety and well-being of subjects until the IRB can assess the research monitor's report.
2. The PI identifies candidates for the position of research monitor, taking into account the nature and disciplinary focus of the study and the likely type of expertise required. The PI attaches to the IRB application curriculum vitas for the proposed monitors and a written summary of the monitors' duties, authorities, and responsibilities.
3. As part of its review, the IRB considers the information regarding the proposed monitor(s) including his/her educational and professional expertise as required by the DoD to provide oversight (See *Definitions* above).
4. The IRB approves the research monitor(s) by name and approves a summary of the monitor's duties, authorities, and responsibilities.
5. The PI provides the IRB with a letter from the monitor accepting the role and associated responsibilities.
6. The PI conveys to the monitor relevant DoD-specific orientation/education requirements of the role (See also *Department of Defense Ethics Education* above.)

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 research monitor promptly reports observations or findings to the ORI and IRB

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Research Involving Vulnerable Populations

1. For research involving subjects defined in 45 CFR 46 Subpart B (pregnant women, fetuses, and neonates), C (prisoners), or D (children), the PI identifies and informs ORI/IRB of any regulatory subpart modifications or limitations imposed by the DoD (as defined in Department of Defense Directive 3216.02) or DoD Component relative to the proposed research.
2. Active duty military and reserve members under the age of 18, (e.g., academy students/trainees) are considered to be adults with legal capacity to participate in DoD supported research. The participation of such members is not subject to Subpart D of 45 CFR 46. However the IRB may consider and determine such members are not necessary or appropriate to include in the proposed research.
3. ORI/IRB submits research requiring any action by an official of HHS about any requirements of subparts B, C, or D to the Assistant Secretary of Defense for Research and Engineering ASD(R&E).

Research Involving International Citizen Populations

1. In the IRB application, the PI provides the necessary information, as appropriate, on the subject populations, the cultural context, customs, practices, and the languages understood by the human subjects.
2. The PI is responsible for identifying national or local laws and regulations, and following them when designing and implementing the research. In the IRB application, the PI includes documentation that research plan is in compliance with applicable local laws and regulations as confirmed by an official of the local government, local IRB, legal counsel or other expert.
3. To ensure the IRB has appropriate knowledge of the local context, the IRB uses an ad hoc or cultural consultant in accord with its standard operating procedures outlined in the Initial Review SOP.

Research Involving U.S. DoD Personnel as Research Participants

1. For research involving clinical investigations, the PI includes women and minority military personnel, unless the DoD component has waived this requirement.
2. In conducting the review, the IRB takes into consideration the unique risks involved in enrolling DoD personnel as research subjects. If the IRB does not have the relevant expertise, ORI obtains consultation from an ad hoc expert with working knowledge of the risks or from the DoD component.

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3. In cases where the research involves U.S. DoD personnel as subjects, the PI submits with the IRB application a subject recruitment plan that incorporates additional safeguards to minimize undue influence from individuals within a potential subject's chain of command. The PI consults the sponsoring DoD Component, as necessary, for assistance.
4. For research involving greater than minimal risk to subjects *and* involving DoD personnel, the PI includes procedures in the subject recruitment plan to ensure that officers cannot influence the decision of their subordinates to participate in the research.
5. The PI includes, in the IRB application, procedures in the subject recruitment plan to ensure that superiors in the chain of command, officers, and senior or other non-commissioned officers cannot be present at the time of recruitment or consent of their subordinates.
6. The PI provides a separate opportunity or recruitment session for supervisors, officers, and senior non-commissioned officers to participate as research subjects.
7. For greater than minimal risk studies involving military service members in which subject recruitment occurs in a group setting, the PI ensures an independent research monitor shall be present during the recruitment and informed consent process to monitor the voluntary nature of participation and ensure that information provided is adequate and accurate.
8. For greater than minimal risk studies involving DoD civilian employees in which subject recruitment occurs in a group setting, the IRB may at its discretion, require an independent research monitor to be in attendance based on the human subject population, consent process and recruitment strategy.

Compensation for Participation in Research

1. The IRB reviews the proposed subject compensation plan to ensure that the PI is aware of DoD policies and limitations depending on whether or not participation occurs during on-duty or off- duty status and whether funds used to compensate subjects come from a Federal source as follows:
 - DoD personnel (active duty and civilian):
 - On Duty: compensation limited to blood draws
 - May participate in research during work or duty hours with supervisor approval and no compensation other than \$50 per blood draw
 - Compensation can be from Federal or non-Federal source
 - Off Duty:
 - No restrictions as long as the source of compensation is not Federal dollars, but compensation for up to \$50 per blood draw can be a from a Federal source

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Non DoD personnel:

- No restrictions and compensation can be from a Federal or non-Federal source.

Waiver of Informed Consent

1. If the research is minimal risk, the IRB may use criteria in (45 CFR 46.116 or 32 CFR 219.116) to approve a waiver of some elements of informed consent.
2. If the research meets the definition of “research involving a human beings as experimental subjects” (as defined in DoD Directive 3216.02), the PI obtains consent from the subject or the subject’s legal authorized representative (LAR).
3. The IRB makes the determination as to whether the research meets the definition of “research involving human beings as experimental subjects.” The IRB shall not approve a waiver of consent if the research includes subjects meeting the definition of “research involving a human being as an experimental subject” unless the DoD has issued a waiver.
4. If consent will potentially be obtained from the subject’s LAR the IRB ensures that the research is intended to be beneficial to the experimental subjects.

Waiver of Informed Consent For Planned Emergency Research

1. As planned emergency research would meet the definition of “research involving human beings as experimental subjects, DoD regulations prohibit a waiver of informed consent in planned emergency research unless the PI obtains approval of the study by DoD and in accordance with DoD Directive 3216.02 .
2. The IRB shall not approve an exception from informed consent in emergency medicine research unless the DoD has issued a waiver.

Classified Research

1. Research involving classified information requires prior approval from the Secretary of Defense. The PI works with the DoD component to determine if information is considered classified; what information will be needed for IRB approval and oversight; and what information subjects will require during the consent process and during research.
2. The PI informs the ORI/IRB regarding specified requirements.
3. Waiver of informed consent is prohibited. As part of the consent process, the PI identifies the DoD as supporting the research, states the research is classified, and explains the extent and impactions of such classification.

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4. The full convened IRB reviews the protocol and determines whether potential human subjects need access to classified information to make a valid, informed consent decision.
5. After IRB approval, the DoD component coordinates the submission for approval from the Secretary of Defense.

Multi-Site or Collaborative Research Requirements

1. A PI developing a proposal for DoD funding or other support that involves other collaborating institutions consults the sponsoring DoD Component and ORI staff early in the proposal development process to identify additional requirements for multi-site research.
2. OSPA staff are responsible for negotiating formal agreements with collaborating institutions (see Office of Sponsored Projects Administration/IRB/ORI SOP). OSPA staff, in conjunction with the PI, ensure that the formal research agreement between participating institutions includes a statement of work and specifies the roles and responsibilities of each party.
3. For collaborative research involving UK and DoD researchers, the UK may choose to rely upon the DoD IRB for review and oversight following the standard operating procedures outlined in the Off-Site Research SOP. For collaborative research involving UK and non DoD institutions, UK follows standard operating procedures outlined in the Off-Site SOP. UK and the collaborating institution sign an IRB authorization agreement which includes a statement of work specifying the roles and responsibilities of the relied upon IRB.
4. In order to ensure consistent protection of subjects under DoD requirements, a PI conducting DoD-sponsored multi-site research submits information to the IRB on the federal assurance(s) held by collaborating institutions, including the existence of any DoD Addendum or other direct DoD assurance.
5. The PI provides the UK IRB additional information to ensure ongoing communication among participating IRBs and sites, as indicated in the Off-Site Research SOP.

Prohibition on Involvement of Detainees in Research

1. Under no circumstances shall the IRB approve research involving detainees as defined in DoD Directive 2310.01, (see *Definitions* above).
2. This prohibition may not apply to certain investigational treatment studies conducted for the purpose of diagnosis or treatment of a medical condition in a patient. The PI works with the DoD component to ensure compliance with limitations of this provision.

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Additional DoD Review Required Prior to Initiation of Study

1. After the IRB completes its review and issues approval, the PI submits documentation of IRB approval, the risk level, and the expiration date of the research to the DoD Component sponsoring or supporting the study.
2. The DoD may also request additional documentation of initial and ongoing to verify compliance with federal and DoD policies, including minutes related to the research. As appropriate, ORI staff provide the PI any additional information pertinent to IRB review, which may not be under a PI's purview. The PI sends requested information to the DoD.
3. The PI may not initiate the study until the human research protection officer (HRPO) within the sponsoring DoD Component reviews and approves the IRB approval and other submitted documentation.
4. If the study is for DoD-sponsored survey research or survey research within the DoD that involves DoD personnel, the PI, with assistance from ORI staff, identifies any requirements for an additional level of DoD review of the study. 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.
5. The PI notifies OSPA and ORI staff upon receipt of relevant HRPO authorization and/or DoD Survey Review approval, as appropriate. OSPA staff establish the account only after receiving certification of final human subjects and survey review and approval from the HRPO or relevant DoD designee.

Reporting and Recordkeeping

1. The PI promptly notifies the HRPO of:
 - IRB approval of significant changes to the research protocol;
 - results of IRB continuing review;
 - subject complaints
 - unanticipated problems involving risks to subjects or others;
 - instances of serious or continuing noncompliance;
 - suspension or termination of IRB approval; and
 - any Federal department or agency or national organization for cause investigation involving a DoD-supported human research protocol.
2. ORI staff make records accessible for inspection by authorized representatives of the DoD and/or supporting DoD Component as specified in the Inspection by Regulatory Agencies SOP.
3. ORI staff secure and maintain IRB records for DoD-sponsored research in accord with the provisions of the IRB-ORI Recordkeeping SOP. In addition, the PI determines, in

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conjunction with ORI, whether the DoD Component requires submission of IRB records to the DoD for archiving. The PI submits the relevant IRB records to the DoD, as appropriate with assistance from ORI staff.

REFERENCES

Department of Defense Directive, DoDD 3216.02, DoDD 2310.01E
32 CFR 219.116