BY ORDER OF THE COMMANDER
AIR FORCE RESEARCH LABORATORY (AFRL)

AFRL INSTRUCTION 40-402

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Medical Command

PROTECTION OF HUMAN SUBJECTS IN RESEARCH

COMPLIANCE WITH THIS PUBLICATION IS MANDATORY

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This instruction describes Air Force Research Laboratory procedures for implementing Air Force Policy Directive 40-4, *Clinical Investigation and Human Use in Medical Research*, and Air Force Instruction 40-402, *Protection of Human Subjects in Biomedical and Behavioral Research*, for research on human subjects conducted or funded by AFRL. It also ensures that AFRL is in compliance with the Code of Federal Regulations, 32 CFR 219, *Protection of Human Subjects*. It directs establishment of Institutional Review Boards (IRBs) to provide ethical review of proposed research and oversight of research in progress. This instruction covers all research on human subjects, which takes place at AFRL facilities, is conducted by AFRL personnel at any location, or is sponsored or supported by AFRL through contracts or collaborative arrangements. Ensure that all records created as a result of processes prescribed in this publication are maintained in accordance with (IAW) AFMAN 33-363, *Management of Records*, and disposed of IAW the Air Force Records Disposition Schedule (RDS) located at **https://afrims.amc.af.mil/**. Refer recommended changes and questions about this publication to the Office of Primary Responsibility (OPR), using the AF IMT 847, *Recommendation for Change of Publication*; route AF IMT 847s from the field through the appropriate functional's chain of command.

SUMMARY OF CHANGES

This instruction has been substantially revised and must be thoroughly reviewed.

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1. Applicability and Scope. This instruction covers all research about human subjects, which takes place at AFRL facilities, is conducted by AFRL personnel at any location, or is sponsored or supported by AFRL through contracts or collaborative arrangements. The guidance provided in this instruction is in addition to the requirements of 32 CFR 219; 10 USC 980; DoDD 3216.02, *Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research;* AFI 40-402; where applicable 21 CFR 50, 21 CFR 56 and 45 CFR 46 (subparts B, C, and D) and any other Federal, State or local requirements applicable to human research. Where policy is clearly stated in these regulations, it may not be repeated in this instruction.

1.1. Tests of Materiel. Research specifically includes the development, test, and evaluation of systems and materiel. Where humans are not the subjects of research, regardless of risk, this instruction will not be applied. Other regulation may apply to these research efforts. Regulation regarding AFRL research test programs is found in AFRLI 61-103 *AFRL Research Test Management*. AFRL directors are responsible for ensuring that any research project involving humans is evaluated by the IRB administrative office or a designated research reviewer (IAW AFI 40-402) to determine if it is human research and subject to IRB oversight.

1.2. Exempt Research. Certain types of investigations are exempt from the requirements of formal IRB oversight as described in 32 CFR 219.101. Principal investigators (PIs) who believe their projects constitute exempt research must have this confirmed in writing by the IRB administrative office or a designated research reviewer before data collection begins IAW paragraph **3.6.** of this instruction.

1.3. Collaborative Research. Studies, which involve collaboration of Air Force investigators with non-Air Force organizations, must comply with procedures in AFI 40-402.

1.4. Research by Contractors. Contracted research on human subjects must fully comply with 32 CFR 219 and Air Force instructions. For internal research performed wholly or in part by DoD personnel, approval by an Air Force IRB must be completed for the study prior to granting of funds. For non-collaborative external research efforts conducted by civilian institutions, IRB approval may come from either an Air Force IRB or another IRB whose institution holds a Federal Wide-Assurance (FWA) and Air Force-Issued DoD Addendum to the FWA.

2. Roles and Responsibilities.

2.1. AFRL Commander (AFRL/CC). The AFRL Commander:

2.1.1. Functions as the Organizational Commander for use of human subjects in research as required by AFI 40-402.

2.1.2. Delegates AFRL Authorized Institutional Official (AIO) duties per AFI 40-402.

2.2. AFRL AIO.

2.2.1. Oversees AFRL IRB compliance with relevant Air Force policy and instructions.

2.2.2. Oversees training and continuing education for AFRL IRB administrators, chairpersons, and members.

2.2.3. Reviews and approves, approves with conditions, or disapproves IRB-approved protocols.

2.2.4. Appoints and removes the IRB chairperson and IRB members. Appointments are valid until removal, but subject to an annual review. The chairperson and members will be appointed in writing to include information that position requirements have been fulfilled or are waived by the appropriate authority. Waiver authority is the Air Force Surgeon General's Research and Oversight Division (HQ USAF/SGRC). Letters of removal will state the reason for removal (e.g., permanent change of station, failure to complete membership requirements, misconduct, etc.).

2.2.5. Supervises AFRL IRB administration.

2.2.6. Reviews any reported adverse event involving a human subject.

2.2.7. Enforces corrective action for any investigators found to be non-compliant with IRB and/or other requirements.

2.3. Institutional Review Board (IRB).

2.3.1. The IRB is established under the authority of the AFRL Commander, IAW AFI 40-402. The IRB functions under the authority outlined in 32 CFR 219.

2.3.2. The purpose of the IRB is to protect the rights and welfare of human research subjects as provided in 32 CFR 219, DoDD 3216.02, and AFI 40-402. Specifically, the IRB ensures that all research on humans conducted or supported by AFRL is accomplished in an ethical manner, that the privacy, comfort, and safety of the subjects are protected to the maximum extent feasible, and that the research is clearly appropriate and fulfills legitimate Air Force requirements that cannot be met through non-human testing. This requires the IRB to make ethical judgments, as well as assessing the scientific quality or merit of the research design.

2.3.3. The IRB monitors compliance of AFRL investigators with all requirements for use of human subjects.

2.3.4. The IRB will ensure that the PIs are aware of AFRL procedures for reporting any adverse event involving a human subject.

2.3.5. The IRB will conduct required reviews of approved protocols IAW AFPD 40-4 and current guidance from HQ USAF/SGRC.

2.4. IRB Chairperson. The IRB chairperson is responsible for the overall operation of the IRB process in terms of ensuring compliance with this instruction and applicable regulations and other requirements per paragraph **1.** of this instruction, (Applicability and Scope). **Note:** The IRB chairperson may be dismissed at any time by the AIO for failure to fulfill responsibilities or misconduct.

2.4.1. Appointment Prerequisites: In addition to the requirements in AFI 40-402, completes initial formal IRB training. This may be a symposium or course sponsored by Air Force Surgeon General's Research Oversight and Compliance Division (HQ USAF/SGRC) or recognized national agencies (such as IRB 101 and IRB Administrator 101 conducted by Public Responsibility in Medicine and Research (PRIM&R)) and the Collaborative Institutional Training Initiative (CITI) training modules required for IRB members and investigators.

2.4.2. Becomes familiar with 32 CFR 219, DoDD 3216.02, and AFI 40-402, as well as this instruction and any other regulations or requirements governing human research.

2.4.3. Ensures that the convened IRB meeting is conducted in a professional manner and that IRB members are given the opportunity to discuss the risks and benefits of research and have their concerns heard in an open and fair environment.

2.4.4. Performs initial review and approval or designates an IRB member to perform an initial review on all protocols submitted to the IRB administrative office.

2.4.5. Reviews and approves the IRB meeting minutes.

2.4.6. Signs the final approval letter to investigators for all approved research.

2.5. IRB Administrator. The IRB administrator is responsible for the day-to-day operation of the IRB administrative office. The administrator should be an expert on Human Research Protection matters, able to assist investigators, the IRB, and leadership in navigating IRB issues.

2.5.1. Completes initial formal IRB training. This may be a symposium or course sponsored by HQ USAF/SGRC or recognized national agencies (such as IRB Administrator 101 conducted by PRIMR) and the CITI training modules required for IRB members and investigators.

2.5.2. Becomes familiar with 32 CFR 219, DoDD 3216.02, and AFI 40-402, as well as this instruction and any applicable DoD, Air Force, or Department of Health and Human Services (DHHS) guidance.

2.5.3. Actively tracks the status of all human research proposals (exempt and non-exempt) submitted to and approved by the IRB. This includes research pending approval and ongoing, active research, as well as closed research.

2.5.4. Maintains required documentation in a case file for each protocol and exempt request, as described in 32 CFR 219.115 and paragraph **3.7.** of this instruction.

2.5.5. Ensures the documentation of convened IRB proceedings are in the form of meeting minutes, as required in 32 CFR 219.115 (a)(2).

2.5.6. Maintains open communication with the PI on all issues surrounding their research, including, but not limited to: courtesy notification to the PI of continuing review, outstanding requirements for review and approval, training requirements, approval notifications, suspension or expiration notifications, and submission of required reports (progress reports, final reports).

2.5.7. Ensures preparation for the monthly IRB meeting to include: notification of IRB members, distribution of materials to IRB members, notification of investigators with a protocol on the agenda, and reservation and preparation of conference room with audio, visual and computer support.

2.5.8. Performs an administrative review of all protocol submissions and ensures that all submission requirements are received before processing for review and approval.

2.6. IRB Member. Appointment as an IRB member is a voluntary additional duty and a privilege.

2.6.1. Completes required initial and annual training as directed by the Director of the IRB per DoDD 3216.02 and AFI 40-402. (See paragraph **5.** of this document.)

2.6.2. Regularly attends and participates in monthly IRB meetings. Members are expected to read all relevant materials prior to each meeting and be prepared to participate in discussion of all issues regarding approval and risk to human subjects.

2.6.3. Declares any conflict of interest and recuses themselves from deliberation and voting when appropriate.

2.6.4. Will not disclose or divulge any confidential, proprietary, or private information that is revealed in the course of protocol review, electronically, or in written form to any third party for any purpose whatsoever.

2.6.5. Notifies the IRB Administrative Office in writing of their intent to leave the IRB with as much advanced notice as possible and will include the reason for leaving.

2.7. Division Chief. The chief of each AFRL division that conducts or sponsors research on human subjects shall assist the IRB administrative office in ensuring compliance of division personnel with this instruction and applicable directives from higher headquarters. Specifically, the division chief:

2.7.1. Ensures that all research with human subjects as defined in 32 CFR 219 is referred to the AFRL IRB for review. No research on humans may be initiated until either final written approval or a letter of exemption is obtained from the IRB administrative office.

2.7.2. Reviews all division human research protocols prior to submission to the IRB. This review shall address the following:

2.7.2.1. Competence of the principal and associate investigators to carry out the proposed research,

2.7.2.2. Scientific merit of the project as ascertained through appropriate peer review,

2.7.2.3. Relevance of the research to meeting valid Air Force needs,

2.7.2.4. Necessity for use of human subjects rather than non-human alternatives,

2.7.2.5. Validity of the experimental design including:

2.7.2.5.1. Articulation of a clear and testable hypothesis.

2.7.2.5.2. Establishment of appropriate data quality control.

2.7.2.5.3. Adequacy of planned statistical analysis.

2.7.2.5.4. Appropriateness of number of experimental subjects, sufficient for statistical validity without use of excessive numbers.

2.7.2.6. Minimization of discomfort and risk to subjects,

2.7.2.7. Adequacy of division safety program and preparedness for medical emergencies, including provision for medical monitoring, procedures for notification of emergency medical personnel, and currency of Cardio Pulmonary Resuscitation or first aid training of division personnel where applicable,

2.7.2.8. Availability of the required personnel and resources, as well as the division's intention to implement the protocol if it is approved.

2.7.3. Establishes division procedures for review of issues in paragraph **2.7.1.**, **2.7.2.**, and above. Divisions will use the IRB supplied cover letter to document division approval of submissions to the IRB.

2.7.3.1. By signing the coordination sheet without exception, the division chief is certifying compliance with all items included in paragraph **2.7.1.** and **2.7.2.** as required by 32 CFR 219, DoD, and Air Force policy.

2.7.3.1.1. If the protocol fails to meet any criterion in paragraph **2.7.1.**, **2.7.2.**, or above, the PI shall attach to the protocol a letter describing the deficiency and justifying the proposal. The division chief shall review this narrative and indicate division concurrence with the request for IRB review despite the deficiency.

2.7.3.1.2. If the division lacks expertise to deal with a specific topic, the division chief shall so note on the cover sheet and shall seek appropriate expertise to guide determinations required.

2.7.4. Immediately evaluates reports from investigators or medical monitors concerning any adverse event involving a human subject to determine whether the protocol should be suspended and notifies the AIO and IRB administrative office within 24 hours of such determination.

2.7.5. Immediately notifies the IRB administrative office of any investigation of scientific misconduct involving an investigator engaged in human research.

2.8. Principal Investigator. The PI for each human research protocol has critically important responsibilities as listed in AFI 40-402. In addition, the PI must:

2.8.1. Understand and comply with 32 CFR 219, DoDD 3216.02, and AFI 40-402, as well as this instruction and any other regulation or requirement applicable to a specific human research protocol (e.g., 21 CFR 50 *Protection of Human Subjects* and 21 CFR 56 *Institutional Review Boards* for FDA studies).

2.8.2. Ensure that all human research, whether conducted under an approved protocol or declared exempt, conforms to the terms of its approval or exemption, including any modifications or restrictions imposed during the review process. Unless necessary to eliminate immediate hazards to subjects, changes to approved research will not be implemented until IRB approval is obtained.

2.8.3. Monitor the progress of research and follow AFRL procedures for reporting any adverse event or unanticipated problem involving a human subject.

2.8.4. Maintain current knowledge of related research through review of published literature and contacts with other scientists.

2.8.5. Promptly notify the IRB administrative office if new information from any source substantially alters the risk/benefit analysis from that represented in the protocol or if partial results clearly show that continued collection of data is no longer warranted. Notify the IRB administrative office and participating subjects immediately of any unanticipated risks or other information which might affect the subject's decision to participate in the study. The PI is required to immediately report to the IRB administrative office and division chief any adverse event or unanticipated problem involving a subject.

2.8.6. Establish the following records for each approved protocol:

2.8.6.1. The original, signed Informed Consent Document (ICD) must be filed with the protocol records. These records must be turned over to the IRB administrator for permanent archiving at the time of continuing review and with the final report.

2.8.6.2. A copy of the signed ICD must be given to each subject.

2.8.6.3. For protocols involving greater than minimal risk, an additional copy of the signed ICD must be filed with the subject's medical records.

2.8.6.4. A case file for each protocol, which must include the following:

2.8.6.4.1. IRB approved protocol and ICD,

2.8.6.4.2. All approval letters from the IRB and HQ USAF/SGRC (where applicable),

2.8.6.4.3. Annual progress reports and/or final report,

2.8.6.4.4. All requested and approved amendments,

2.8.6.4.5. Adverse events or unanticipated problems,

2.8.6.4.6. Any Assurance of Compliance approved by HQ USAF/SGRC and any Individual Investigator Agreements (IIA) when applicable, and

2.8.6.4.7. Copies of the division and PI cover letters.

2.8.7. Provide to the IRB administrative office an annual listing of scientific publications and presentations relating to each approved human research protocol, including those already terminated.

2.8.8. Must provide sound justification for waiver of requirements in 32 CFR 219, DoDD 3216.02, AFI 40-402, or this instruction.

2.8.9. Investigator failure to comply with responsibilities or requirements may lead to suspension of IRB approval for the protocol until the lapse has been corrected and reinstatement is approved by IRB and the AIO.

3. IRB Procedures.

3.1. IRB Membership.

3.1.1. IRB membership will conform to the requirements outlined in 32 CFR 219.107 and DoDD 3216.02.

3.1.2. The IRB chairperson along with the IRB administrator will periodically (at least annually, but as often as necessary) review IRB membership regarding the recruitment, retention, or dismissal of members. This review includes examination of attendance, specialty, expertise, education, affiliation, and diversity. Following this review, recommendations for appointment or dismissal are made to the AIO.

3.1.3. The AIO will formally appoint or dismiss members in writing.

3.1.4. There is no specific term (length) of appointment. The IRB membership will be reviewed at least annually and adjusted as appropriate.

3.1.5. Appointment as an IRB member is a privilege, not an entitlement. An IRB member may be dismissed at any time for failure to fulfill responsibilities delineated in this instruction, paragraph **2.6.**

3.1.6. The IRB may call upon outside consultants as necessary for additional expertise on a particular population or area of research. Outside consultants are not voting members and are expected to maintain the confidentiality of the research.

3.2. IRB Meetings.

3.2.1. Schedule. A convened IRB meeting will be held at least once per month for review of research that does not qualify for expedited review. The submission deadline for review at an IRB meeting is four weeks prior to the date of the meeting. All submission requirements must be received by this date in order for a protocol to be considered at the meeting. Non-scheduled meeting may be convened to review research or other emergent issues. Scheduling of an emergency meeting depends entirely on the schedule of IRB members and the ability to obtain a quorum.

3.2.2. Agenda. The IRB chairperson may bring any issue to the convened IRB meeting, which he/she deems appropriate for consideration and voting. In addition to the review of new and continuing research protocols, the agenda will include a

monthly training topic, a list of research approved through expedited procedures, research that was reviewed and considered to be exempt, adverse events, and a quality assurance section. The quality assurance section will include information on spot-checking of active research and issues of noncompliance or misconduct.

3.2.3. Voting. A period of discussion and the voting of IRB members is conducted without the investigators in attendance. Investigators never participate in the voting process. Voting will follow a formal motion which has been followed through with a second. If there is no second to a motion, there will be no vote and the motion will not be considered approved. Votes will be tallied by a show of hands and statement of the word "Aye." All those in favor, opposed, and abstaining from voting will be recorded. The reasons for individual members voting against a motion (opposed) must also be documented in the minutes. While all members with an opinion on a motion should register a vote, they cannot be compelled to do so. A member may choose to abstain for any reason, such as where the member feels uncomfortable voting for or against a motion. Note that an abstention may count as a vote against a motion. Any IRB member with a conflict of interest is recused from the discussion and voting process and must leave the room for the final discussion and vote (see paragraph **12.** of this instruction). When a member is recused from discussion and voting on a protocol, that person does not count in the tally of voting members present towards a quorum for that protocol. In the event that a recusal should reduce the number of members present to below a quorum, the IRB may still discuss a protocol, but may not vote to approve it; the protocol will be automatically tabled until the next IRB meeting for voting. A motion will be considered approved if it receives a simple majority of votes in favor of approval.

3.3. Initial Review. A new protocol submitted to the IRB administrative office for review will follow the review sequence outlined below. A submission will not be considered complete until the IRB has received all of the required items specified in paragraph **3.3.1.**

3.3.1. Submission requirements. The following items are required for each protocol submitted to the IRB administrative office and must conform to the format and instructions provided for each document. Current templates and instructions for completing these forms can be found on the IRB web site or obtained from the IRB administrator. Once these items are received, the protocol will be considered for review and approval.

3.3.1.1. Signed directorate cover letter,

3.3.1.2. Signed PI cover letter,

3.3.1.3. Research protocol,

3.3.1.4. Informed Consent Document,

3.3.1.5. Assurance of compliance,

3.3.1.6. Proof of completed human research protection training (must be current within 1 year) for all investigators and key research personnel, and

3.3.1.7. Curriculum vitae for investigators.

3.3.2. Administrative review. All proposals submitted to the IRB administrative office will be reviewed first by an IRB administrator to ensure that the protocol, ICD, and all required supporting documentation are complete. Once administrative review is complete, the IRB administrator will forward the protocol and pertinent supporting documents to the IRB chairperson or designee for review.

3.3.3. Primary review. The IRB chairperson or designee will conduct the initial review of all protocols. This review will consist of the following determinations:

3.3.3.1. Human research definitions. A determination is made if the proposal consists of human research based on the definitions provided in 32 CFR 219.102 (d) and (f), as well as AFI 40-402. If a protocol or activity is determined to be research that does not involve human subjects or is not research at all, a written determination will be provided to the PI that includes an explanation as to why the proposal does not meet the defined criteria for human research. No further IRB review or oversight will ensue for projects that are determined not to be human research.

3.3.3.2. Risk level. The risk to subjects for participation in the research is evaluated based on the procedures involved and the definition of risk provided in 32 CFR 219.102 (i). If there is any question that a protocol may be greater than minimal risk, it will be scheduled for review at the convened meeting.

3.3.3.3. Review category. One of three review categories will be assigned: exempt, expedited, or convened IRB review. If the protocol is deemed minimal risk by the reviewer, a determination will be made if it may be exempt or reviewed through expedited review procedures. Even though the protocol may qualify for exemption or expedited review, the reviewer may assign a higher level of review (expedited or convened IRB, respectively) if he/she deems necessary.

3.3.4. See paragraph **3.6.** of this instruction, Exempt Research, for details regarding the Exempt review category.

3.3.5. Expedited review. If the research falls into one of the categories of expedited review designated by the Department of Health and Human Services and meets the criteria in 32 CFR 219.110, it may be reviewed by expedited-review procedures. The

IRB chairperson or designee will perform all expedited review or appoint an IRB member to conduct expedited review. Following initial review of the protocol, the reviewer will communicate concerns and/or conditions of approval to the PI. The PI will respond with a revised protocol and explanation or clarification of any issues of concern raised by the reviewer. The reviewer may refuse to approve a protocol through expedited procedures if he/she feels that the PI is not adequately addressing concerns or refuses to comply with conditions of approval. The reviewer may exercise all of the authorities of the IRB except for recommendation for disapproval. In this case, the research will be referred to the convened IRB for consideration. The date the IRB Chair or designee signs the IRB approval letter is the official approval date for an expedited protocol.

3.3.6. Convened IRB review. If the protocol does not meet the criteria for expedited review and is not exempt, it will be scheduled for review at the next convened IRB meeting IAW the deadlines in paragraph **3.2.1.** of this instruction. At the convened meeting, the IRB will:

3.3.6.1. Determine if the research involves minimal or greater than minimal risk to subjects.

3.3.6.2. Determine the frequency of continuing review to be conducted on at least an annual basis. The IRB may determine that continuing review should be earlier than one year based on specific risks to subjects or circumstances of the research involved.

3.3.6.3. Approve, approve with conditions, table, or disapprove reviewed research for another meeting. The date of the IRB meeting at which the protocol is approved or approved with conditions will be the official approval date of a full-board protocol.

3.3.6.3.1. Approved means accepted as written with no conditions.

3.3.6.3.2. Approved with conditions means the protocol is approved pending explicit minor changes. All explicit conditions requested must be completed and documented before final IRB approval will be released. For these conditions, the IRB chairperson or designee can, upon reviewing the PI's response(s) to the conditions, approve the research on behalf of the IRB.

3.3.6.3.3. Tabled means that no voting occurs and the protocol is delayed until a future meeting pending changes. Generally, the protocol, ICD, or other materials have deficiencies that prevent accurate determination of risks and benefits or require significant

clarifications, modifications or conditions that, when met or addressed, require convened IRB review and approval of the PI's responses and revisions.

3.3.6.3.4. Disapproved means that as proposed, the protocol describes a research activity that is deemed to have risks which outweigh potential benefits, protocol is significantly deficient in several major areas, or otherwise does not comply with applicable requirements referenced in paragraph **1.** of this instruction. Investigators will be notified in writing of disapproval, the reason(s) for disapproval, and provide instructions for how to appeal the determination. A protocol that is disapproved may be resubmitted if the protocol is revised to address all reasons for IRB disapproval.

3.3.7. Legal review. Written legal review is obtained for all non-exempt research to ensure that the protocol and ICD are congruent with human-use law and regulations and any other law or regulation (Federal, DoD, Air Force, or otherwise) that may be applicable to specific components of the research.

3.3.8. Institutional review. Once the protocol has been approved by the convened IRB or through expedited review, it is forwarded to the AIO for review and determination IAW paragraph **2.2.4.** The AIO receives a letter of approval from the IRB chairperson or designee for expedited protocols or a copy of the meeting minutes for protocols approved at the convened meeting. Letters of exemption are also forwarded to the AIO for concurrence.

3.3.9. HQ USAF/SGRC review. After Institutional review and approval, all non-exempt research is forwarded to HQ USAF/SGRC for review. If the research is approved as greater-than-minimal risk by the IRB or requires an Assurance of Compliance to be issued by HQ USAF/SGRC, final approval will not be issued to the PI until HQ USAF/SGRC review is complete. In addition, all international research, regardless of exemption status, will be forwarded to HQ USAF/SGRC for review and approval prior to final approval being issued.

3.3.10. Final approval/disapproval. Final approval of research is issued to the PI in writing only after all of the above steps have been completed. Final written approval will include a statement that requires the investigator to obtain IRB approval before implementing changes and report adverse or unanticipated events to the IRB administrative office. The final approval will also include the date of IRB approval, the date at which IRB approval will expire, and the date continuing review will be due. If research is disapproved either by the IRB or AIO, the PI will be notified in writing to include an explanation as to why the research was not approved.

3.4. Continuing Review. Unless determined otherwise by the IRB, all approvals are valid for the period of 365 days. This is determined from the date of approval (date of the meeting at which a protocol was approved by the convened IRB or the date the approval

letter to the AIO is signed by the IRB for expedited review). The IRB does not have authority to extend the term of approval for each protocol beyond one year under any condition. The date upon which a protocol approval term ends is referred to as the expiration date.

3.4.1. Frequency of review. A determination will be made upon initial IRB approval regarding the appropriate term of approval for each protocol. Per 32 CFR 219, continuing review must be accomplished on at least an annual basis. In order to ensure continuing review is conducted at least on an annual basis, continuing review will generally be due 11 months from the date of IRB approval unless otherwise specified by the IRB. A progress report, (see AFRL IRB website for the template) original signed ICDs (the PI may retain a copy for their research records), and an amended research protocol (if amendments are requested) must be turned in to the IRB administrative office 30 days prior to the date for continuing review indicated on IRB approval letter. For example, a protocol initially approved on 3 January 2008 for a term of 1 year would be scheduled for IRB review in December 2008, and the progress report would be due to the IRB on 3 November 2008; the IRB approval of the study would expire on 2 January 2009 if continuing review had not been performed. Though the IRB administrative office sends PIs courtesy notifications of impending review and expiration of protocols, it is ultimately the responsibility of each PI to ensure required documentation is submitted to the IRB in a timely manner.

3.4.2. Expiration of IRB approval. If IRB approval of continuing review is not completed within the term of approval set by the IRB, the protocol will expire. The IRB administrative office will issue a letter notifying the PI of the expiration and instructing that all human research activities must be suspended until the research can be reviewed and approved.

3.4.3. Determination of outside verification. The IRB may require verification outside that of the investigator that no changes have occurred in the protocol since the previous IRB review. For example, this may be accomplished for protocols where the investigator has had the current or other protocols suspended for non-compliance in the past year.

3.5. Amendments. Any change to a research protocol or the ICD must be submitted to the IRB administrative office as a written request. The amendment request must follow the established format (see AFRL IRB website for the template) and include any revised or new study documents (e.g., the Protocol, ICD, or advertisements) with all changes marked as an attachment. No change to a protocol or ICD may be implemented without prior IRB approval. In general, amendment requests to a protocol will be reviewed at the same level as the initial protocol unless they qualify for expedited review.

3.6. Exempt Research. Each proposal submitted to the IRB administrative office will be considered for exemption whether submitted as a specific exempt request or as a full research protocol. If a full research protocol qualifies for exemption, the PI will be notified and given the opportunity to pursue exemption if they so desire. If a request for exemption

is denied, the PI may be notified in writing, and given the opportunity to pursue expedited or convened board review.

3.6.1. Submission requirements. Research activities that may be categorized as exempt IAW 32 CFR 219.101(b) can be submitted to the IRB via an exemption request letter in lieu of a full protocol. The exemption request letter must contain sufficient information about the research activity to determine if it is exempt or not. If utilizing the AFRL IRB process, the exemption request letter must follow the established format (see AFRL IRB website for the template). In addition to the exemption request letter, the following are required before submission of an exemption request:

3.6.1.1. Completion of AFRL human subject protections training is required for all investigators.

3.6.1.2. A directorate cover letter must be included if the research is being conducted or sponsored by AFRL.

3.6.1.3. If the proposal involves international research, a letter of exemption from an IRB in the country where the research is to be executed must be submitted. This letter must specifically state that the proposed research is considered exempt or not normally subject to IRB or regulatory oversight by local laws and standards.

3.6.2. Each exemption request will be reviewed by the IRB chairperson or designee. A written determination will be provided to the investigator stating whether or not the proposed activity is exempt.

3.7. Records. The IRB administrator will maintain a case file for each protocol or exempt request submitted to the IRB administrative office. These records will be retained indefinitely. Each case file will include:

3.7.1. IRB approved protocol and ICD;

3.7.2. All approval letters from the IRB, AIO, and HQ USAF/SGRC (where applicable);

3.7.3. Annual progress reports and a final report;

3.7.4. All requested and approved amendments;

3.7.5. Adverse events or unanticipated problems;

3.7.6. All correspondence between the PI and the IRB administrative office;

3.7.7. IRB minutes for the meeting where the research was reviewed/approved;

3.7.8. Any Assurance of Compliance approved by HQ USAF/SGRC or an individual investigator assurance where applicable;

3.7.9. Documentation of legal review;

3.7.10. Division and PI cover letters;

3.7.11. Curriculum vitae of investigators;

3.7.12. Original Signed ICDs;

3.7.13. Presentations or publications resulting from the research submitted by the PI; and

3.7.14. Investigations of non-compliance to include final outcome.

3.8. Appeal of an IRB decision. A principal investigator has the right to appeal any decision made by the IRB. Appeal of an IRB decision must follow the procedures outlined below.

3.8.1. The appeal must be for the IRB to reconsider a decision.

3.8.2. The decision must be opinion-based (does not violate law/regulations).

3.8.3. The appeal is made in writing within 30 days of written notification of the IRB's decision.

3.8.4. The appeal will be reviewed by the IRB. The IRB will invite the investigator to the IRB meeting if the IRB has additional questions for the investigator. The IRB will reconsider its decision. The second decision is final.

3.8.5. No one has the authority to override an IRB disapproval. Only the IRB can decide to reconsider a decision. If an appeal is considered by the IRB, the following actions are available: 1) let previous decision stand; 2) reverse all or part of the previous decision.

3.9. Protocol Closure. When human subjects research under an approved protocol is complete, a final report is required to close the protocol. Research under a particular protocol is considered to be complete when the study is closed to the enrollment of new subjects and all data collection and analysis of identifiable data are complete. A study cannot be closed by the IRB administrative office without a report from the PI confirming that research is complete, and there is no further interaction with human subjects or their private identifiable information. At this time, the originals of any signed ICDs not turned

in at the time of continuing review must also be submitted to the IRB. If a protocol is reviewed but never fully approved, a final report is not required.

3.10. Suspension or Termination of IRB Approval. Only the convened IRB has the authority to disapprove or terminate approval of research. The IRB chairperson may suspend approval of research that has expired without notification of the IRB or HQ USAF/SGRC. The IRB chairperson may suspend approval of research for other reasons (potentially serious or continuous non-compliance, subject safety or welfare, etc.) pending a final determination at the convened IRB. Suspension of approval for any reason other than expiration of continuing review requires written notification to the investigator, Division Chief, AIO and HQ USAF/SGRC. The written statement will include the IRB's reason for suspending or terminating approval.

3.11. Vice Chairperson. A vice chairperson(s) may be appointed by the AIO in writing. The vice chairperson must be an IRB member and be familiar with the day-to-day operations of the IRB administrative office, and may be assigned other IRB-related duties as needed. The vice chairperson has the authority to act on behalf of the chairperson and must fulfill the responsibilities as delineated in paragraph **2.4.** of this instruction. In the rare event that both the chairperson and vice chairperson are temporarily unable to fulfill their duties, the chairperson may appoint an IRB member as his/her designee on a temporary basis. This appointment must be in writing, for a specified period of time, and with specific delineation of authorities.

4. Medical Monitoring of Protocols. Medical oversight of protocols is provided by a qualified healthcare provider IAW DoDD 3216.02, paragraph **4.4.3.** Medical monitoring should be accomplished by a person sufficiently removed from the research at hand to provide objective analysis and oversight of medical risks. The IRB administrative office will ensure that the medical monitor or medical consultant is appropriately qualified to serve in such a capacity based on the nature of the research and the level of risk involved. The investigator and medical monitor have the responsibility of suggesting the level of monitoring needed for a specific protocol. The IRB has responsibility to determine what level of monitoring oversight will occur. Definitions and responsibilities for different types of medical oversight are provided below.

4.1. Medical Consultant. All human subjects research, at a minimum, must have a medical consultant. A medical consultant is most appropriate for minimal risk studies that have few if any medical risks and do not require any direct medical observation during data collection. The division originating the protocol must obtain medical review and approval before the protocol is submitted to the IRB. This reviewer shall:

4.1.1. Determine, along with the PI, what risks and discomforts are anticipated in the research. The risks and discomforts may be physical, psychological, or a breach of confidentiality.

4.1.2. Assure that protocol design minimizes risk, discomfort, and psychological stress to subjects, and that appropriate provisions are made for protection of privacy and confidentiality. Where a Health Insurance Portability and Accountability Act of

1996 (HIPAA) covered entity is involved, ensures that the appropriate HIPAA waiver or permission for release is obtained.

4.1.3. Determine that the protocol specifies appropriate medical procedures to screen out potential subjects with preexisting conditions or pathology that would result in greater than normal risk.

4.1.4. Assure that division equipment, procedures, training, and personnel are adequately prepared to meet any medical emergency that might occur during the testing of human subjects.

4.2. Medical Monitor. All greater than minimal risk research must have a medical monitor. The medical monitor bears the overall responsibility for medical and subject advocate oversight on a protocol. The medical monitor and medical consultant may be the same individual. In addition to the responsibilities of a medical consultant, the medical monitor will:

4.2.1. Determine the level of on-site medical observation, with the concurrence of the IRB, which is required for the research. Depending on the nature of the risks involved during the experiment, a medical observer may be required to be on call, in the same building, or continuously present and in communication with the subject. Some greater-than-minimal risk research may require on-scene medical observation. If the medical monitor does not personally provide this observation, then the monitor is responsible to design an appropriate system to provide observation. This includes selection and training of the observers. The observer in this system may be a physician, technician, or other health professional as found to be appropriately qualified by the monitor.

4.2.2. The medical monitor (or consultant) is required to report to the IRB and division chief any adverse event involving a subject. The report should include the medical monitor's/consultant's recommendation as to whether or not the protocol should be suspended pending further investigation.

4.2.3. The medical monitor must be credentialed at a DoD or civilian medical facility and have an active state medical license.

4.3. Medical Observer. The medical monitor is not required to directly oversee data collection sessions, but may appoint one or more qualified medical observers to directly monitor subject safety during data collection. The medical monitor may serve as an on-site medical observer. The duties of an on-site medical observer include:

4.3.1. Immediate termination of any experiment if the subject's vital signs exceed acceptable levels or if it appears that the subject is at increased risk,

4.3.2. First response to any adverse event involving the subject,

4.3.3. Notify the medical monitor immediately of any unanticipated problem, subject injury, or adverse event.

5. Training

5.1. Human Research Training. All investigators and key personnel involved in the conduct of human research (exempt or non-exempt) are required to complete with a passing score, human research protection training prior to submitting a protocol or exempt request to the IRB administrative office.

5.2. Initial and Recurrent Annual Training Requirements. Both initial and recurrent annual training for investigators will consist of the designated AFRL modules on the Collaborative Institutional Training Initiative (CITI) web site.

5.3. Annual Training. Training is required annually. Failure of any investigator or key personnel on the protocol to complete annual human subjects training may result in suspension of IRB approval for that protocol.

5.4. Continued Education of IRB Members. A continued education topic for IRB staff and members will be included as standard agenda for each IRB meeting. The nature and content of this training is at the discretion of the IRB chairperson.

5.5. Institutional Officials, IRB Members, and Staff Training. Training for institutional officials, IRB members, and staff will consist of initial and annual completion of the required AFRL modules on the CITI web site. Additional training requirements are listed under "Roles and Responsibilities" for respective positions.

6. Adverse Events and Unanticipated Problems.

Research should be designed in such a way as to minimize the occurrence of adverse events. However, adverse events and unanticipated problems that involve risk to subjects or others will arise. It is crucial that investigators and medical monitors take the appropriate steps in evaluating and reporting any adverse event or unanticipated problem. While the medical monitor should be closely involved, it is ultimately the responsibility of the PI to report adverse events and take the appropriate corrective action.

6.1. Adverse Events. An adverse event is any untoward or unfavorable medical occurrence (physical or psychological) in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. There are several types of adverse events defined in AFI 40-402.

6.1.1. Serious adverse events. A serious adverse event results in death, threat to life, limb or eyesight, inpatient hospitalization (or prolongation thereof), persistent or significant disability/incapacity, a congenital anomaly or based upon appropriate

medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

6.1.2. Unexpected adverse events. Any untoward experience not identified in the risks and discomforts section of the protocol and ICD.

6.1.3. Important medical events. An important medical event is an incident, experience, or outcome that is neither serious nor unexpected, but may have an impact on risk to subjects or others and warrants evaluation and reporting.

6.2. Unanticipated Problems Involving Risk to Subjects or Others. An unanticipated problem may not meet the criteria for an adverse event. An unanticipated problem is any incident, experience, or outcome that meets all of the following criteria:

6.2.1. Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and ICD; and (b) the characteristics of the subject population being studied;

6.2.2. Related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

6.2.3. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

6.3. Reporting of Adverse Events and Unanticipated Problems. All reports of adverse events or unanticipated problems must follow the established format and be submitted in writing. Reports from the IRB to the AIO and HQ USAF/SGRC may be included in the meeting minutes with the attached report from the PI.

6.3.1. The investigator must report any adverse event that is both serious and unexpected to the IRB as soon as possible but within 72 hours from the time the event is recognized.

6.3.2. All serious adverse events or unanticipated problems must be reported to the IRB as soon as possible but within seven working days of recognition.

6.3.3. All adverse event reports will be reviewed at the convened IRB meeting. The IRB will either accept the report as submitted, request additional information or require additional corrective actions to be taken, to include suspension or termination of IRB approval. The IRB may also request a follow-up report at a specified interval. If approval of the protocol has already been suspended or research temporarily halted, the IRB will determine if, and under what conditions or modifications, the research

may resume. Documentation of the review will be recorded in the IRB Meeting Minutes.

6.3.4. The AIO will be notified of all adverse events and unanticipated problems in the IRB meeting minutes.

6.3.5. The IRB must report any adverse event that is both serious and unanticipated to the HQ USAF/SGRC as soon as possible but within 15 working days of notification.

6.3.6. Principal Investigators may be required to notify other agencies of Adverse Events or Unanticipated Problems (e.g., Detachment Safety Office IAW AFI 91-204, Para **6.1.**, etc.). Timelines for these reporting requirements may vary from IRB requirements. Investigators are responsible to ensure they know and adhere to these requirements.

7. Non-compliance. Non-compliance is different from scientific misconduct which is addressed in paragraph **8.0**. of this instruction. Non-compliance may be intentional or unintentional. All allegations of non-compliance are taken very seriously and will be investigated in a fair, thorough, and objective manner with every effort to maintain the confidentiality of those involved.

7.1. Definitions.

7.1.1. Non-compliance is defined as any violation of any regulation that governs human subject research, the failure on the part of an investigator conducting human research to comply with the requirements of the IRB or any deviation from the study documents (e.g., protocol, ICD, recruiting material, etc.) approved by the IRB.

7.1.2. Minor non-compliance does not impact subject safety, compromise the integrity of the study or data, violate a subject's rights or welfare, or affect the subject's willingness to participate in the research.

7.1.3. Serious non-compliance may impact subject safety, compromise the integrity of the study or data, violate a subject's rights or welfare, or affect the subject's willingness to participate in the research

7.1.4. Continuing non-compliance is defined as a series of more than one non-compliant event, in reasonably close proximity, that indicates the need for evaluation of methods and systems used to protect human subjects.

7.2. Initial Investigation. All allegations of non-compliance in human research will be initially reviewed and investigated by the IRB chairperson. The IRB chairperson will determine if there was minor, serious, or continuous non-compliance involved. The IRB chairperson may refer any case of alleged non-compliance to the IRB for any reason. If at

any point during the investigation of non-compliance it appears that scientific misconduct may also be present, procedures in paragraph **8.0.** of this instruction will be followed.

7.3. Referral to the IRB. If the IRB chairperson determines that the non-compliance is potentially serious or continuing, the case will be referred to the convened IRB. The IRB will review the facts gathered by the IRB chairperson and any information submitted by the investigator. The investigator will be offered the opportunity to speak to IRB members at the meeting to present any information in person. The IRB will then determine the nature of non-compliance (serious or minor) and agree upon a corrective action.

7.4. Notification of Action.

7.4.1. Serious or continuous non-compliance. The AIO will be notified of the IRB's final recommendation regarding corrective action to be taken. The AIO will consider the recommendation and decide on an appropriate course of action.. Following AIO disposition, the PI along with his/her branch and division chief will be notified in writing of the corrective action.

7.4.2. Minor non-compliance. If the IRB chairperson determines that minor non-compliance is involved, the PI and the PI's Branch Chief will be notified in writing. Written notification will describe the nature of the non-compliance and include any corrective action that is required.

7.4.3. Appeals may be made IAW paragraph **3.8.** of this instruction.

7.5. Reporting to HQ USAF/SGRC. All events that are found to be serious or continuing non-compliance will be reported promptly to HQ USAF/SGRC.

7.6. Records. All records regarding the investigation of non-compliance, including facts gathered, correspondence, IRB minutes, letters to the AIO, and letters to the investigator will be filed in the corresponding protocol case file.

8. Scientific Misconduct. Scientific misconduct is defined in AFI 40-402 as the fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. All allegations of scientific misconduct will be investigated and resolved IAW AFI 40-402 and DoDD 3210.7 *Research Integrity and Misconduct*. The additional procedures outlined below apply only if the alleged misconduct involves human research. All allegations of scientific misconduct are taken very seriously and will be investigated in a fair, thorough, and objective manner with every effort to maintain the confidentiality of those involved.

8.1. Division Chief Responsibilities. The Division Chief will notify the IRB chairperson immediately if, following an inquiry, an investigation of scientific misconduct is initiated on an investigator.

8.2. IRB Chairperson Responsibilities. If the potential for scientific misconduct arises during an investigation of non-compliance, the IRB chairperson will immediately notify the Division Chief of the investigator(s) involved.

8.3. Determination of Violations. The IRB chairperson will assist the Division Chief in determining if human research subject rights were violated or harm to subjects resulted from the misconduct. If the IRB chairperson determines that subjects were harmed or their rights were violated as a result of the misconduct, the case will be referred to the IRB for consideration. If the IRB chairperson determines that subjects were not harmed and their rights were not violated, this will be documented in writing to the Division Chief and the investigation will continue IAW AFRL/RH OI 61-01.

8.4. Review of Alleged Scientific Misconduct. IRB review of alleged scientific misconduct will follow the same procedures outlined for alleged cases of non-compliance in paragraphs **7.3.-7.6.** of this instruction. Any corrective action imposed by the IRB will be in addition to any requirements following the investigation conducted under procedures in AFRL/RH OI 61-01.

9. International Research. International research is defined as research that is conducted at a facility outside of the continental United States and involves research subjects that are not U.S. citizens. In addition to the standard submission requirements, international research will require review by an IRB or other ethics committee that reviews human research in the local community of the country in which the research is to be conducted. Whenever possible, this committee should satisfy the IRB membership requirements outlined in 32 CFR 219.107. This IRB or ethics committee must be able to review the research and ensure that it is acceptable based on national and local requirements, standards, and norms. This committee must also be willing to serve in an oversight capacity to assist the AFRL IRB in any matters of compliance and oversight. The AFRL IRB must be provided with the informed consent documents in the native language, as well as a back-translated version for review. All international research, regardless of risk level or determination of exemption, must be reviewed and approved by AF/SGRC (the Surgeon General's Human and Animal Research Panel (SG HARP)) prior to commencement.

10. Quality Assurance. The IRB administrative office will conduct random spot checks of approved research to ensure compliance. Any IRB member can perform a quality assurance visit, except where any potential conflict of interest exists. A quality assurance visit will consist of a one-on-one interview with the PI, and possibly the research staff, and completion of the audit form (see AFRL IRB website for the template). Observation of the informed consent process or data collection may also be accomplished at the discretion of the person conducting the visit. The PI will be given a copy of the audit form following the visit and an informal verbal explanation of the results. The results of all audits will be reviewed at the convened IRB meeting, after which the PI will be notified in writing of the final results, any deficiencies, and any corrective actions that may be required.

11. Subject Recruiting Policy. Federal Guidelines consider direct advertising for study subjects to be the start of the informed consent and subject selection process. All recruitment materials or methods (e.g., ads, flyers, e-mails, briefings, telephone recruitment scripts, etc.) *must* be reviewed and approved by the IRB as part of the package for initial review. The IRB will review the information contained in the recruitment material and the mode of its communication to determine that the recruiting procedures are appropriate, not coercive. The protocol must contain sufficient detail on the recruiting procedures (e.g., who will do the recruiting, when and how it will be done, etc.) to allow this determination to be made.

11.1. Preventing Coercion. Special attention to preventing coercion must be addressed in the protocol when recruiting military subjects. It must be made clear that commanders and supervisors will not be involved in the recruiting process in *any* way. Personnel in a position of authority must not promote participation or be present during subject recruiting briefings nor will they be made aware of who does and does not volunteer. For more information, refer to DoDD 3216.02.

11.2. Subject Recruitment. Generally, any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest. The AFRL IRB, therefore, requires that advertisements be limited to the following information, as recommended in FDA guidance regarding subject recruitment:

11.2.1. The name and address of the investigator and/or research facility,

11.2.2. The condition under study and/or the purpose of the research,

11.2.3. In summary form, the criteria that will be used to determine eligibility for the study,

11.2.4. A brief list of participation benefits, if any,

11.2.5. The time or other commitment required of the subjects, and

11.2.6. The location of the research and the person or office to contact for further information.

11.3. Reimbursement. When reimbursement will be provided to subjects, it can be stated in the advertisement that subjects will be compensated for time, travel, and inconvenience.

12. Conflicts of Interest Definition. A conflict of interest refers to situations in which financial or other personal considerations may adversely affect, or have the appearance of adversely affecting, an individual's professional judgment in exercising any duty or responsibility related to the design and execution of research or other professional activities.

12.1. Conflict of Interest. All personnel involved in the conduct or oversight of human research have a responsibility to identify and eliminate or mitigate any potential conflict of interest and fully disclose to subjects that such a conflict exists when it cannot be eliminated. The IRB chairperson will remind members at the beginning of each meeting to declare any conflict of interest and recuse themselves from voting where appropriate**.** The ICD shall list all sponsors of the research and any potential conflict of interest that has not been eliminated.

12.2. Notification for Potential Conflict of Interest. Investigators will notify the IRB administrative office in writing of a potential conflict of interest on any given protocol. Financial relationships in general do not need to be disclosed; only specific information as it relates to a given research protocol.

12.3. Financial Interest. A financial interest means anything of monetary value and includes but is not limited to the following:

12.3.1. Salary or other payments for services (e.g., consulting fees, honoraria, gifts, or employment with an outside organization);

12.3.2. Equity interests (e.g., stocks, stock options, or other ownership interests);

12.3.3. Intellectual property rights (e.g., patents, copyrights, and royalties from such rights);

12.3.4. Membership on a governing board.

12.4. Conflict of Interest and Senior Leadership. To avoid a conflict of interest, or the perception of such, senior members of organizations (e.g., Division Chiefs and their deputies as well as Branch Chiefs and their deputies) who are also members of the IRB, will abstain from voting when protocols from their Divisions/Branches are being presented.

12.5. Appearance of Conflict. The mere appearance of a conflict may be as serious and potentially damaging as an actual distortion of instructional, research, or administrative goals, processes, or outcomes. Apparent conflicts, therefore, should be disclosed and evaluated with the same vigor as actual conflicts.

13. Protocol Design. Good protocol design is the key to minimizing the risks of human research. The goal of the design and review process is to see that the smallest possible number of subjects is exposed to the lowest possible level of risk and discomfort while still meeting the objectives of the research. The experimental objective must clearly justify the use of human subjects.

13.1. Risk Reduction. Techniques include use of existing knowledge, use of alternative methods that do not involve human subjects, statistical design to use the fewest possible subjects, medical screening of subjects, medical observation during experiments, and implementation of a laboratory safety program.

13.2. Format. The protocol and ICD templates and instructions are designed to ensure that all of the required information is included in the protocol. Protocol and ICD format is required to follow the established template. Use of the most current templates and instructions available on the AFRL IRB web site is strongly recommended**.**

14. Approval and Oversight Authorities. In addition to the AFRL IRB, there are other levels of research oversight within the Air Force and the DoD.

14.1. AFRL IRB. The IRB administrative office is the first level of approval and oversight authority for research conducted or supported by AFRL. All final written approval to investigators to begin research comes from this office.

14.1.1. Protocols involving minimal risk. If the IRB approves a protocol as minimal risk, research may begin once written approval is received from the IRB administrative office. The protocol and records of its approval are forwarded to HQ USAF/SGRC for their review and records. If the protocol requires an Assurance of Compliance, it must be approved before research can begin.

14.1.2. Protocols involving greater-than-minimal risk, non-lethal weapons, and international research. Protocols of this type require approval by HQ USAF/SGRC before they can begin. This may involve review of the research by the Surgeon General's Human and Animal Research Panel (SGHARP).

14.2. HQ USAF/SGRC. The Air Force Surgeon General's Research Oversight and Compliance Division (HQ USAF/SGRC) is the final approval authority for all human research conducted or supported by AFRL. All non-exempt research is submitted to HQ USAF/SGRC and may be subject to required modifications or requests for additional information. HQ USAF/SGRC is also the approval authority for all Air Force-Issued DoD Assurances of Compliance. This office does not have an IRB but performs headquarters review for compliance issues. When needed, the SGHARP will review research deemed controversial or high-risk in addition to the research designated for its review by AFI 40-402.

14.3. Director, Defense Research and Engineering (DDR&E). In the Office of the Deputy Under Secretary of Defense for Science and Engineering, Biosystems Directorate, the Assistant Director for Regulatory Affairs oversees the establishment and execution of policy related to research involving human subjects. This office maintains oversight over each of the DoD component's second level review (HQ USAF/SGRC).

15. Prescribed and Adopted Forms.

15.1. Prescribed Forms:

None.

15.2. Adopted Forms:

None.

MICHAEL L. CARLSON
Colonel, USAF
Chief of Staff

Attachment 1

GLOSSARY OF REFERENCES AND SUPPORTING INFORMATION

References

10 USC 980, *Limitations on Use of Humans as Experimental Subjects,* 1 October 1985

21 CFR 50, *Protection of Human Subjects* (FDA), 1 October 2003

21 CFR 56, *Institutional Review Boards* (FDA), 1 April 2002

32 CFR 219, *Protection of Human Subjects* (DoD), 1 July 2006

45 CFR 46 (subparts B, C, and D), *Protection of Human Subjects* (DHHS), 1 October 2003

Air Force Instruction 40-402, *Protection of Human Subjects in Biomedical and Behavioral Research,* 5 May 2005

AFRL/RH OI 61-01, *Research Ethics,* 12 July 2006

AFRLI 61-103, *AFRL Research Test Management,* 1 November 2007

Air Force Policy Directive 40-4, *Clinical Investigation and Human Use in Medical Research,* 11 May 1994

DoDD 3210.7, *Research Integrity and Misconduct,* 14 May 2004

DoDD 3216.02, *Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research,* 25 March 2002

Acronyms

AFRL - *Air Force Research Laboratory*

AIO - *Authorized Institutional Official*

CITI - *Collaborative Institutional Training Initiative*

DHHS - *Department of Health and Human Services*

DoD - *Department of Defense*

FDA - *Food and Drug Administration*

FWA - *Federal Wide Assurance*

HIPAA - *Health Insurance Portability and Accountability Act of 1996*

ICD - *Informed Consent Document*

IRB - *Institutional Review Board*

PI - *Principal Investigator*

PRIM&R - *Public Responsibility in Medicine and Research*

SGHARP - *Surgeon General's Human and Animal Research Panel*