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SECRETARY OF THE AIR FORCE**

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Medical Command

**PROTECTION OF HUMAN SUBJECTS IN
BIOMEDICAL AND BEHAVIORAL
RESEARCH**

COMPLIANCE WITH THIS PUBLICATION IS MANDATORY

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This instruction implements AFPD 40-4, *Clinical Investigation and Human Use in Medical and Biomedical Research*. It provides guidance and procedures for conducting research investigations at medical treatment facilities (MTFs), clinical investigation facilities (CIFs), and other medical support centers and for using human subjects in research, development, test, and evaluation (RDT&E) conducted or funded by the Air Force. For programs using animals, refer to AFJI 40-401, *The Use of Animals in DoD Programs*. "This instruction directs collecting and maintaining information subject to the Privacy Act of 1974 authorized by 10 U.S.C. 55 and 10 U.S.C. 8013. System of Records F044 AF SG E, Medical Record System, applies." "Manage and dispose of records resulting from prescribed processes in accordance with AFMAN 37-139, *Records Disposition Schedule*." Send comments and suggested improvements on AF Form 847, **Recommendation for Change of Publication**, through channels, to AFMOA/SGOT, 110 Luke Avenue, Room 405, Bolling AFB DC 20332-7050.

(USAFA) Air Force Instruction (AFI) 40-402, Protection of Human Subjects in Biomedical and Behavioral Research, 5 May 2005, is supplemented as follows: The Office of Primary Responsibility (OPR) for this supplement is HQ USAFA/A9N. This supplement provides guidance for the use of human subjects in research, development, test, and evaluation (RDT&E) conducted or funded by the Air Force. It applies to all United States Air Force Academy (USAFA) personnel, or those who wish to use USAFA members as research participants or wish to conduct research with human participants. This publication does not apply to US Air Force Reserve, Air National Guard, and/or Civil Air Patrol units or members. This instruction directs collecting and maintaining information subject to the Privacy Act of 1974 authorized by 10 U.S.C. 55 and 10 U.S.C. 8013. Apply the following System of Records F044 AF SG E, Medical Record System or F061 AFMC A, Aeromedical Research Data. Refer recommended changes and questions about this publication to the Office of Primary Responsibility (OPR) using the AF Form 847, Recommendation for Change of Publication. Ensure that all records created as a result of processes prescribed in this publication are maintained in accordance with AFMAN 33-363, Management of Records, and disposed of in accordance with the Air Force Records Information Management System (AFRIMS) Records Disposition Schedule (RDS) located at <https://www.my.af.mil/gcss-af61a/afrims/rims.cfm>. See Attachment 1 for a glossary of references and supporting information.

SUMMARY OF CHANGES

This instruction supplements 32 CFR 219; 45 CFR 46, Subparts B-D (as adopted by DoDD 3216.2; being under the authority of DoD, the "Secretary of Defense" shall be substituted for the "Secretary of Health and Human Services" throughout); 21 CFR 50, 56, 312, and 812; 10 USC 980; DoDD 3216.2 and DoDD 6000.8. When two or more rules are applicable, the most stringent shall take precedence. This IC changes the name of the publication from *Protection of Human Subjects in Biomedical and Behavioral Research* to *Protection of Human Subjects in Research* (title page); updates OPR office symbol from AFMOA/SGOT to AFMSA/SGRC (throughout); updates the OPR and certified by lines (title page); clarifies that this instruction applies to all human research conducted or supported by the Air Force (paragraph 1.1); details roles and responsibilities of the Surgeon General and includes training requirement (paragraph 2.1); details roles and responsibilities of the Surgeon General's Research Oversight Committee and includes training requirement (paragraph 2.2); details roles and responsibilities of AFMSA/SGRC and includes training requirement (paragraph 2.3); clarifies responsibilities of the commander and his Authorized Institutional Official (AIO), includes training requirement (paragraph 2.5.1); states AIO responsibilities related to review of research misconduct (paragraph 2.5.7); details roles and responsibilities of the Institutional Review Boards, including training requirement and reporting to AFMSA/SGRC (paragraph 2.6); (paragraph 2.7.1.1); includes investigator responsibilities for training (paragraph 2.7.1.1); updates information on Assurances of compliance, including requirements for AFMSA/SGRC approval prior to implementation of change in Assurances and coordination of non-Air Force Assurances through AFMSA/SGRC (paragraph 3.1); details information on the International Single Project Assurance (paragraph 3.1.2.3); clarifies requirement to comply with 45 CFR 46, Subparts B-D, for certain vulnerable populations (paragraph 3.2); clarifies the unequivocal prohibition against using prisoners of war as human subjects (paragraph 3.2.4.1); clarifies that research with biological or chemical warfare agents is generally prohibited (paragraph 3.2.6); updates SGROC

procedures for review of protocols (paragraph 3.6.1); updates information on research misconduct as per DoDI 3210.7 (paragraph 3.9.1); and clarifies obligation of contractors for requirements of prior approval of any protocol changes prior to implementation (paragraph 4.1.7).

PROTECTION OF HUMAN SUBJECTS

(USAFA) This revision changes HQ AF/SGRC to AFMSA/SGEC throughout the document. Paragraph 2.5. changes USAFA/XPX to USAFA/A9N and changes the name to Strategic Plans and Programs, Requirements, Assessments, and Analyses. Paragraph 2.6.1. changes the appointment term for Commandant of Cadets Representative from 2-years to 3-years, and changes the quorum amount to 6. Paragraph 2.6.1.4. changes Professional Standards to Medical Standards. Paragraph 2.6.1.6. changes CW to Commandant of Cadets. Paragraph 2.6.1.8. adds the IRB administrator as a voting member. Paragraph 2.6.2. adds the requirement for training done on an annual basis. Paragraph 2.6.4.3. adds that a memo for record will be signed by the AIO after each meeting. Paragraph 2.6.4.4. added the process for Appeals if disapproved by the AIO. Paragraph 2.7.16. changes the website address for the IRB. Paragraph 2.7.19.2. adds information relating to Cadets under Age 18. Paragraph 2.7.19.3. adds information for the payment of cadets who participate in research. Paragraph 2.7.20. adds information on pilot studies.

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Chapter 1

SCOPE

1.1. Description. In 1991, the DoD, along with 16 federal agencies, adopted regulations that are known collectively as the Common Federal Rule. Title 32, Code of Federal Regulations, Part 219, "Protection of Human Subjects" applies to all research conducted or supported by the DoD. The Department of Health and Human Services' corollary is Title 45, Code of Federal Regulations, Part 46, Subpart A. These regulations embody the ethical principles of the Belmont Report and the World Medical Association Declaration of Helsinki. This instruction supplements 32 CFR 219 and the Food and Drug Administration's (FDA) complimentary regulations, 21 CFR 50 and 56, and is intended to describe laws, regulations, policies and practices that are unique to research conducted or supported by the U.S. Air Force (USAF). This instruction applies to all human subject research conducted or supported by the Air Force. It applies to research that includes human subjects, whether as the direct object of research or as the indirect object of research in the development and testing of military weapon systems, vehicles, aircraft, and other material. It applies to research activities funded by non-Air Force resources in which the human subjects are Air Force military or civilian personnel. It also applies to Air Force funded studies and non-Air Force funded studies at U.S. military installations.

1.2. Research. Research, as defined in this instruction, does not include individual or group training of military personnel such as combat readiness, effectiveness, proficiency, or fitness exercises.

Chapter 2

RESPONSIBILITIES

2.1. The Surgeon General

2.1.1. Is the single point of accountability for the Air Force Human Research Protection Program (HRPP).

2.1.1.1. Completes human subjects protection training established by AFMSA/SGRC.

2.1.1.2. Is responsible for ensuring Air Force compliance with all applicable human subjects protection requirements. Appoints a Surgeon General's Research Oversight Committee (SGROC). Delegates authority to SGROC and AFMSA/SGRC to monitor compliance of the HRPP; this authority cannot be further delegable.

2.1.1.3. Authorizes funds to support the Air Force Clinical, Biomedical, and Behavioral Investigations in accordance with DoDD 6000.8

2.1.1.4. Provides blanket authorization for Air Force medical center participation in the National Cancer Institute's (NCI) Clinical Trials Cooperative Group Program.

2.1.1.5. Shall serve as the final authority on implementation of DoD Instruction 3210.7, Research Integrity and Misconduct. Delegates this function to the lowest possible organizational level that allows an independent, unbiased, and equitable process. Reserves the right to exercise authorities that otherwise would be delegated to local Air Force institutions.

2.1.2. May grant deviations from this instruction consistent with applicable law and supported by adequate justification.

2.2. The Surgeon General's Research Oversight Committee (SGROC)

2.2.1. Ensures compliance with federal policy for the protection of human subjects (32 CFR 219; 45 CFR 46, Subparts B-D; 10 USC 980; DoDD 6000.8; DoDD 3216.2; 21 CFR 50, 56, 312, and 812; and all other applicable requirements related to human subjects protection).

2.2.1.1. Completes human subjects protections training established by AFMSA/SGRC.

2.2.2. Approves, recommends changes, defers or disapproves all research protocols of greater than minimal risk and all amendments to approved protocols adding significant risk, with the exception of cooperative group oncology studies, for which SGROC either concurs with IRB approval, concurs with changes recommended, or non-concurs. Has the authority to determine exempt status of proposed research activities when deemed necessary and appropriate. Ensures compliance of all other protocols as per paragraph 3.6.1 of this instruction. Reviews serious, unexpected, related adverse event reports and forwards acknowledgement and any necessary recommendations to the IRB in a timely manner.

2.2.3. Renders final decision on all protocols involving investigational use of drugs, devices, and radiopharmaceuticals prior to the initiation of the study. Submit appeals to AFMOA/SGOT Division Chief for reconsideration.

2.2.4. Coordinates on emergency-use protocols and submits approval, disapproval, and recommendations to the institution for implementation or action.

2.2.5. Has the authority to suspend or terminate research projects in Air Force institutions to assure protection of human subjects.

2.3. The Research and Compliance Office (AFMSA/SGRC)

2.3.1. Is the Air Force administrator for Institutional Assurances of Compliance (Assurances) IAW the Federal Policy for the Protection of Human Subjects. Coordinates, approves and monitors Assurances for all human research conducted or supported by the Air Force. Has the authority to suspend or terminate Assurances in cases of serious non-compliance.

2.3.2. Establishes policies on human subjects protections training to be completed on at least an annual basis by headquarters level personnel, AFMSA/SGRC, SGROC members, and oversight staff to ensure compliance of the Air Force Human Research Protection Program (HRPP). Completes training on at least an annual basis. Ensures that all personnel connected with the human subjects research review process (including but not limited to AFMSA/SGRC staff, the Surgeon General, the Assistant Surgeon General, Modernization, IRB members, IRB administrative staff, investigators, and key research personnel) understand and are qualified to meet their obligation to protect the rights and welfare of human subjects by requiring completion of human subjects protection training prior to involvement with any human research.

2.3.3. Reviews offers of gifts and grant applications for research investigations that exceed the delegated authority of AFI 51-601, *Gift to the Air Force*, and processes them through the Office of the Secretary of the Air Force for final approval.

2.3.4. Coordinates policy and provides guidance for human research and interprets regulations for the HRPP. Is responsible for keeping the DoD (via DDR&E or designee) informed of significant issues regarding the safety of human subjects, including:

2.3.4.1. Any suspension or termination of a DoD Assurance issued by the Air Force or of any other assurance submitted by the Air Force to another federal entity;

2.3.4.2. Any investigation of the Air Force conducted by an outside entity;

2.3.4.3. Any investigation of a grantee by the Air Force that results in negative findings; and,

2.3.4.4. Significant communication between the Air Force and other federal departments and agencies regarding compliance and oversight.

2.3.5. Monitors funds in support of clinical, biomedical and behavioral research projects as described in section 5.1 below.

2.4. Major Command (MAJCOM).

2.4.1. Air Mobility Command (AMC) operates a Clinical Investigation Facility (CIF) in conjunction with the 60th Medical Group (David Grant Medical Center), and a Clinical Investigation Program (CIP) at the 89th Medical Group (Malcolm Grow Medical Center).

2.4.2. Air Force Materiel Command (AFMC) oversees the research and operates an IRB in support of a CIP for the 74th Medical Group (Wright-Patterson Medical Center) and the Air Force Research Laboratory (AFRL).

2.4.3. Air Education and Training Command (AETC) operates CIF's in conjunction with the 81st Medical Group (Keesler Medical Center) and the 59th Medical Wing (Wilford Hall Medical Center).

2.4.4. United States Air Force Academy (USAFA) operates an Institutional Review Board supporting research initiatives.

2.5. Medical Facility Commander (MTF/CC), Organizational Commander, Authorized Institutional Official (AIO).

2.5. (USAFA) Medical Facility Commander (MTF/CC), Organizational Commander, Authorized Institutional Official (AIO). The Authorized Institutional Official (AIO) for the HQ USAFA Institutional Review Board (IRB) and all matters related to the ethical treatment of human research participants is the HQ USAFA Vice Superintendent (HQ USAFA/CV). The HQ USAFA Strategic Plans and Programs, Requirements, Assessments, and Analyses (HQ USAFA/A9N) provides implementation and administration.

2.5.1. Is responsible for ensuring the institutions' compliance with requirements of 32 CFR 219, DODD 3216.2 and this instruction. Alternately, the commander may designate a member of the executive staff to serve as the AIO. The commander or AIO completes on at least an annual basis human subjects protection training established by local policy. The AIO provides a local institutional environment that identifies and strives to reduce the possibility for conflict of interest by personnel responsible for protecting human subjects.

2.5.1. (USAFA) The Surgeon General's Research Oversight & Compliance Division (AFMSA/SGEC) has officially delegated the authority to approve and monitor human research at HQ USAFA to HQ USAFA/CC via the USAFA Multiple Project Assurance. The USAFA/CC delegates the authority to the USAFA/CV with a letter. AFMSA/SGEC reviews USAFA IRB decisions and provides continuing oversight of local IRB operations.

2.5.2. Sends AFMOA/SGOT written assurance of compliance as outlined in section 3.1 of this instruction before conducting non-exempt research projects.

2.5.3. Provides resources and administrative staff to establish an IRB or develops a support agreement with a regional military IRB for review of proposed human research.

2.5.4. Refers any controversial protocols on which the IRB needs additional guidance in the use of human subjects to AFMOA/SGOT.

2.5.5. Approves or disapproves protocols after review by an IRB. If the IRB recommends safeguards or special conditions for a protocol, the commander or designee may not reduce these safeguards or conditions before approving the protocol. The commander or designee may require additional safeguards, disapprove the protocol, or refer the protocol to a higher authority (SGROC). The commander or designee may not approve a project that the local IRB recommends for disapproval.

2.5.6. Ensures processes are in place to evaluate the scientific merit, experimental design, and military relevance of the research protocol.

2.5.7. Establishes local written procedures for review of allegations of research misconduct IAW DoDI 3210.7 and this instruction. Reviews any allegations of research misconduct and determines administrative or punitive actions under the Uniform Code of Military Justice. Ensures research activities will be conducted with integrity and according to ethical and legal

standards. (Refer to Office of Science and Technology Policy letter published in the Federal Register: October 14, 1999, Volume 64, Number 198, pages 55722-55725). See paragraph **3.9** of this instruction.

2.5.8. Ensures all protocols involving the use of radioactive material is forwarded to the local Radiation Safety Office (RSO) to determine if Radiation Safety Committee (RSC) review is required.

2.5.9. Restricts, suspends, or ends a IRB's use of the expedited review procedure when necessary to protect the rights or welfare of subjects.

2.5.10. Ensures process is in place and establishes written policy to collect and archive research records.

2.6. Institutional Review Board (IRB). The IRB's requirements are outlined in 32 CFR 219.107 to 109. Additionally, an Air Force IRB:

2.6.1. Establishes written policies and procedures on human subjects protections training, to be completed by the Institutional Official, IRB members, IRB staff, investigators, and key research personnel on at least an annual basis. Submits training policies to SGROC for approval.

2.6.1. (**USAFA**) The Administrator ensures completion of human subjects protection training prior to allowing any person to conduct human subject research or related protection activities. Training will be accomplished on an annual basis.

2.6.1.1. Ensures completion of human subjects protection training prior to allowing any person to participate in human subject research or related protection activities.

2.6.2. Requires the IRB chairperson to have at least one year of experience as a member of an IRB and demonstrated comprehensive knowledge of applicable regulations for protecting human research subjects.

2.6.3. Ensures that protocols for the use of investigational drugs and devices comply with Food and Drug Administration (FDA) regulations. In addition, a physician who is a voting member of the IRB must be present when an Investigational New Drug (IND) or Investigational Device Exemption (IDE) protocol is reviewed.

2.6.4. Determines if study is exempt and documents exemption status on Optional Form 310, Protection of Human Subjects, Assurance Identification/ Certification/ Declaration (OF 310), section 8, IAW 32 CFR 219.101. Evaluates risk level (minimal risk or greater than minimal risk) of the study and documents in the IRB minutes. If the subject does not have the capacity to provide consent, discussion of the prospect benefit must be documented in the minutes.

2.6.4. (**USAFA**) Exempt Research. Research involving human subjects may be exempt from IRB oversight.

2.6.4.1. (**Added-USAFA**) Final determination of exempt status for all research may only be made by the IRB. A summary of the proposed research and justification for exemption (citing the exemption criteria in 32 CFR 219) should be submitted through the researcher's chain-of-command (departmental or unit) to the IRB Administrator or Research Reviewer. The Chairperson (or another board member designated by the

chairperson) or USAFA Research Reviewer will review the summary and consult with other IRB members as appropriate in making the determination as to exempt status. The researcher will be notified in writing after the determination of exemption status. The summary and the determination will be presented to the full IRB for discussion and comment at the next convened meeting of the IRB.

2.6.4.2. **(Added-USAFA)** When a protocol is approved pending changes, the IRB administrator will forward a letter delineating the required changes to the Principal Investigator (PI). The Administrator will assign a minimum of two members to review the changes submitted by the investigator. The investigator may not execute the protocol until the conditions specified by the IRB have been satisfied and the IRB Administrator has notified the investigator in writing that final approval has been granted.

2.6.4.3. **(Added-USAFA)** Following each IRB meeting, the AIO will sign an approval/disapproval Memo for Record for the protocols that were reviewed at that meeting. The meeting minutes and all reviewed protocols are then sent to the AIO for approval/signature and then forwarded to AFMSA/SGEC.

2.6.4.4. **(Added-USAFA)** Appeals of IRB Decisions:

2.6.4.4.1. **(Added-USAFA)** Appeals must be received within 30 days of written notification of the IRB's decision. The appeal will be considered by the IRB at the next regularly scheduled board meeting. Investigators filing appeals are strongly encouraged to attend the board meeting at which their appeal will be heard.

2.6.4.4.2. **(Added-USAFA)** All appeals should be addressed to the IRB Chairperson and sent to the IRB Administrator at HQ USAFA/A9N. The appeal should address reasons for disapproval and provide substantive information (e.g. new information) for why the board should reconsider the decision.

2.6.4.4.3. **(Added-USAFA)** No one has the authority to override 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) affirm the decision; (2) reverse all or part of the previous decision; or (3) defer opinion until further information can be obtained.

2.6.4.4.4. **(Added-USAFA)** If the AIO disapproves a study based on what is best for the institution and the study was approved by the IRB for the protection of human subjects, then the appeal will be sent to the AIO for review.

2.6.4.4.5. **(Added-USAFA)** If the appeal is disapproved by the AIO and the board then the protocol will be closed. The PI can send in a new revised study using another protocol number.

2.6.4.4.6. **(Added-USAFA)** The PI will be notified in writing of the results of the IRB meeting at which the response was considered.

2.6.5. Defines the research focus area per AFMOA/SGOT guidance.

2.6.6. Determines frequency of continuing review of each research study IAW 45 CFR 46.109(e) (not to exceed 365 days).

2.6.7. Forwards review recommendations to the Commander or the AIO for approval or disapproval.

2.6.8. Completes OF 310 for all protocols approved by the IRB and forwards to AFMOA/SGOT as appropriate. For OPRR approved Cooperative Protocol Research Programs (CPRP) the IRB documents the valid Cooperative Project Assurance (CPA) or Multiple Project Assurance (MPA) number in section 8 of the OF 310.

2.6.9. Reviews Adverse Event (AE) Reports, expected or unexpected, as soon as possible after discovery and reports those that are serious and unexpected to the MTF/CC or AIO. The IRB will review the incident and determine if a change in the research study or ICD is warranted and document follow-up action and reporting by the PI. Reports Adverse Events to AFMOA/SGOT within 15 days that are serious, unexpected, and related to the study using FDA MedWatch Form 3500 or equivalent ([Attachment 5](#)).

2.6.10. Reports substantive issues to AFMSA/SGRC, including, but not limited to:

2.6.10.1. Upcoming inspections by the Department of Health and Human Services (DHHS) or FDA when notified and provides inspection results within 30 days of receipt to AFMSA/SGRC;

2.6.10.2. Any suspension or termination of any assurance submitted by the Air Force to another federal entity;

2.6.10.3. Any investigation of the Air Force conducted by an outside entity;

2.6.10.4. Any investigation of a grantee by the Air Force that results in negative findings; and,

2.6.10.5. Significant communication between the Air Force and other federal departments and agencies regarding compliance and oversight.

2.6.11. Appoints an independent medical monitor by name when the IRB determines the research to be greater than minimal risk. The IRB is responsible for determining the extent of active involvement required of the medical monitor. This determination will be based upon the severity of potentially adverse events and the probability that such events may occur. Ensures the Medical Monitor is identified in the consent document.

2.6.12. Appoints at least annually, an individual(s) to randomly select and spot-check active research study records and consent processes. For Example: this review may include a review of subject eligibility, compliance with the IRB approved protocol, and observation of the consent process. Reports of these spot checks will be provided in writing to the IRB chairperson and discussed and documented at an IRB meeting. IRB's will establish written procedure for this review.

2.6.13. Ensures when a principal investigator is reassigned, separated, or retired, the investigator submits a final report, or requests a change of principal investigator to the IRB.

2.6.14. Maintains official files documenting review, approval, conduct, adverse events, continuing review and final reports, protocol, ICD and changes of the investigations involving human subjects. Requirements are outlined in AFI 37-138 and AFMAN 37-139.

2.6.15. Ensures protocols involving exposure to ionizing radiation, radiopharmaceuticals, or biologically hazardous materials are approved by the appropriate committee prior to IRB approval.

2.6.16. **(Added-USAFA)** Either the primary or alternate IRB member is to attend the IRB meetings. Members must respond to the IRB administrator at least 5 days prior to the scheduled meeting on who will and will not attend. A quorum consists of representatives from 6 of the 10 IRB categories in attendance with one being a scientist and one being a non-scientist. HQ USAFA/CV appoints all IRB members with a letter to AFMSA/SGEC. Appointment terms are as follows: Cadets second class are appointed for a 1-year term and Cadets third class are appointed for a 2-year term. All remaining IRB members are appointed for a 3-year term. All terms are renewable by HQ USAFA/CV. Removal of an IRB member for disciplinary reasons requires recommendation from the IRB Chairperson and a letter from HQ USAFA/CV. For each of the categories below, the HQ USAFA/CV may choose to appoint one or more individuals to the IRB. The exact number of IRB members, therefore, may vary. At USAFA, the IRB is composed of the following categories:

2.6.16.1. **(Added-USAFA)** The Chairperson and Vice-Chairperson. The Chairperson presides over the monthly IRB meeting. The Chairperson has the authority to assign IRB members as expedited reviewers.

2.6.16.2. **(Added-USAFA)** Institutional Policy. At least one member of the IRB must have the background and experience necessary to assist the IRB in understanding those aspects of USAFA organization, policies, procedures, and past practice essential to a full consideration of issues relevant to human research.

2.6.16.3. **(Added-USAFA)** Legal. At least one IRB member must be an attorney. This member provides expert advice to the IRB in interpreting applicable legal standards.

2.6.16.4. **(Added-USAFA)** Medical Standards. At least one IRB member must be a medical professional, preferably a physician. This member advises the IRB on clinical and medical practice issues and professional standards.

2.6.16.5. **(Added-USAFA)** Scientist. At least one IRB member must be a scientist. This member is normally an experienced principal investigator (PI) who advises the IRB on issues of scientific methodology and professional standards.

2.6.16.6. **(Added-USAFA)** Commandant of Cadets Representative. At least one permanent party member of the Commandant of Cadets will serve on the IRB to advise the IRB on Cadet Wing policies, procedures, and issues pertinent to cadet participation in human research.

2.6.16.7. **(Added-USAFA)** Non-affiliated. At least one member of the IRB must have no official connection with USAFA. This member provides a disinterested perspective to the IRB and represents the community's interests.

2.6.16.8. **(Added-USAFA)** The IRB Administrator. The Administrator serves on the IRB to advise on policies and procedures. The USAFA IRB has determined that this is a voting position.

2.6.16.9. **(Added-USAFA)** Cadet. At least one cadet will serve on the IRB to ensure that the interests of cadets, the primary source of participants in human research at USAFA, are represented.

2.6.17. **(Added-USAFA)** Researchers outside USAFA wishing to use USAFA personnel as research participants must obtain a USAFA sponsor and comply with all aspects of this supplement. Research investigators and Department Heads are responsible for making the determination as to whether an activity is research involving human subjects. For the purposes of this supplement, the term “Department Heads” refers to the heads of the academic departments in the Dean of Faculty (DF), the medical departments in 10 MDG, and to other officials at the two-letter level. If there is any possibility that the activity is research involving human subjects, research investigators should seek assistance from the IRB Administrator, Research Reviewer or IRB members in making this determination.

2.6.18. **(Added-USAFA)** The policy of the USAFA IRB is to review all protocols at the monthly meetings. However, if circumstances require review prior to the next convened meeting, some research may be eligible for expedited review IAW 32 CFR 219.111.a3. A summary of the protocol expedited review analysis, and risk determination will be provided to the full board at the next convened meeting of the IRB. Protocols that are not recommended for approval under the expedited review process will be submitted to the full IRB for consideration.

2.7. Principal Investigator (PI).

2.7.1. Ensures compliance with all applicable requirements and is solely responsible for the research project.

2.7.1.1. Completes, and requires research personnel to complete, initial and ongoing human subjects protection training established by the IRB.

2.7.2. Prepares the research protocol (**Attachment 2, Attachment 3**) and, as required, an Informed Consent Document (**Attachment 4**) and submits them to the Commander (or designee) through an appropriate IRB.

2.7.2. **(USAFA)** If appropriate, prepares the research exemption and submits it to the IRB administrator. The IRB administrator will forward it to the Research Reviewer, IRB Chair or other IRB members for review.

2.7.3. Ensures the subject has the capacity to consent, is able to exercise true freedom of choice without overt or hidden persuasion, and is fully informed. If the subject does not have the capacity to consent, see section **3.5.1**. If the subject does not have the capacity to consent, the research must be expected to benefit the subject and consent must be obtained from a legal guardian.

2.7.4. Verifies that an IND or IDE is appropriately coordinated with the FDA according to 21 CFR, and the IND/IDE number is included in the research protocol document. Maintains records and submits reports required by the FDA, when conducting studies as part of an IND or IDE. See paragraph **3.6.3** of this instruction.

2.7.5. Performs and supervises the conduct of the investigation and records data relating to the investigation as required. The principal investigator must provide research records, in

accordance with local policy, to the institution upon completion of the research project or upon reassignment, which ever occurs first.

2.7.6. Documents the medical and dental care given to the subject as part of the study. Gives a copy of the ICD to the subject and adheres to local policy for ICD filing requirements.

2.7.7. Submits all proposed changes to IRB for review and approval prior to implementation in accordance with 32 CFR 219.103(b)(4). Substantive changes require prospective review and approval by the AIO. Notifies the IRB of unanticipated problems with ongoing research in a timely manner.

2.7.8. Submits continuing reviews and final report as required by the IRB. The principal investigator is responsible to inform the IRB of change in his/her status and to arrange for a new principal investigator who is approved by the IRB to continue the project, or to request closure of the protocol. All publications will be submitted to the IRB for inclusion in the protocol records. ([Attachment 8](#)).

2.7.9. Reports serious adverse events, (expected or unexpected), to the IRB Chairperson or designee within five duty days of the event's discovery using FDA MedWatch Form 3500 or equivalent ([Attachment 5](#)).

2.7.10. Provides follow-up to the IRB IAW local IRB policy for adverse event reporting. Coordinates the findings of adverse events with the medical monitor and proposes protocol change to the IRB as needed to minimize risks to other subjects.

2.7.11. Ensures that apparatus, instruments, and personnel are available to deal with medical emergencies. Additionally, the PI will ensure that medical treatment will be provided IAW DoDD 6000.8 (a) 4.9.2.

2.7.12. For investigations using emergency drugs or devices the using physician is the agent responsible for following the FDA-prescribed requirements and must comply with all FDA procedural requirements (specified in 21 CFR 50, 56, 312 & 812) for emergency use of an Investigational Drug or Device. Consistent with 10 U.S.C. 980, under no circumstances can waiver of documentation of informed consent be granted (21 CFR 50.24. does apply to emergency research conducted in the USAF).

2.7.12.1. The PI must submit a formal request for approval ([Attachment 6](#)) to the MTF commander, describing the life-threatening situation and why the absence of standard acceptable treatment is not adequate or appropriate. When possible, obtain the approval prior to using the drug or device. The PI must submit this approval and the request for emergency use to the IRB within 5 workdays of the decision to use the drug. The IRB reviews whether the emergency use is appropriate, makes recommendations as needed to MTF personnel, and sends the request for emergency use, with the MTF commander's approval and the IRB recommendations, to AFMOA/SGOT.

2.7.13. Submits protocols involving exposure of subjects to ionizing radiation, radiopharmaceuticals, or biologically hazardous materials to the appropriate committees prior to IRB review.

2.7.14. Ensures the research is conducted in an ethical manner and the data are reported appropriately. See section [3.9](#).

2.7.15. Maintains study records (signed informed consent documents, IRB communications, approvals, amendments, continuing reviews, etc.) while affiliated with the institution. Upon reassignment or closure of the study the PI will transfer said records to the institution.

2.7.16. **(Added-USAFA)** Meeting dates and protocol submission deadlines are announced on the IRB website (<http://www.usafa.edu/superintendent/xp/xpx/irb/index.cfm>) and posted 6 months in advance. IRB meetings are open to all interested parties although the IRB may conduct certain business in Executive Session (without outside observers) as appropriate. IRB members can request review of any protocol by one or more special consultants. Principal investigators or their representatives should make every effort to attend the IRB meeting at which their protocol will be considered. Past practice has shown that delays in approval are minimized when the investigator is available to answer questions or make clarifications for IRB members.

2.7.16.1. **(Added-USAFA)** A protocol package must be submitted to the IRB Administrator not less than 10 days prior to the date of the IRB meeting at which the protocol is to be considered. If the package contains a survey as the data collection instrument, the package must be submitted 15 days prior to the date of the IRB meeting at which the protocol is to be considered. The package must contain a hardcopy version of the protocol with original signatures, an electronic form of the protocol, and 13 hardcopies of the protocol for IRB member distribution.

2.7.16.2. **(Added-USAFA)** Research investigators must use the protocol template and informed consent document officially approved by AFMSA/SGEC. The most recent versions of these are posted on the IRB website. Any questions regarding format or content of protocols or Informed Consent Documents (ICD) may be addressed to the IRB Administrator. Additional guidance to assist investigators in the preparation of materials for submission to the IRB is posted on the IRB website, currently located at <http://www.usafa.edu/superintendent/xp/xpx/irb/index.cfm>. Since these documents are occasionally revised, the research investigator must use the current website version of these documents each time a new protocol is prepared.

2.7.17. **(Added-USAFA)** When an investigator requests expedited review, the request will include a justification endorsed by the investigator's Department Head.

2.7.18. **(Added-USAFA)** The research investigator should receive a letter from the IRB Administrator within 5 workdays stating the results of the expedited review.

2.7.19. **(Added-USAFA)** Guidelines for Investigators at USAFA. Certain aspects of the unique environment existing at USAFA call for special concern and attention on the part of the investigator wishing to use human subjects as part of a research protocol. This is particularly true when researchers use cadets as subjects. Cadets are considered a vulnerable population. Cadets are potentially vulnerable to coercion in their role as students and as military members. Researchers must take special care to ensure the cadets are aware that their decision to consent or decline to participate in any research project will result in neither adverse nor favorable consideration by instructors in their classes or by others in their military chain of command. Research participants may volunteer to participate in research only after they have been afforded the opportunity to consent or decline to participate in accordance with governing directives.

2.7.19.1. **(Added-USAFA)** Cadet Investigators. Projects conducted by cadets to satisfy course requirements where data collection is confined to cadets within the course is not subject to IRB review. It is the responsibility of instructors and Department Heads to ensure that appropriate consideration is given to ethical issues in the conduct of these projects. However, activities that do fit the definition of research, such as a USAFA 499 class or other higher level cadet research project, are subject to the same IRB oversight as other research. The IRB Chairperson, Vice Chairperson and Administrator are available for consultation or advice regarding these issues. Research conducted in combination with or as part of class projects is not exempt from IRB oversight automatically; the criteria in paragraph 2.6.4. must be met for exemption. If these criteria are not met, then a protocol must be submitted to the IRB.

2.7.19.2. **(Added-USAFA)** Cadets under Age 18: Every year, a few four-degrees enter USAFA who are not yet 18. Under AFI 40-402, Attachment 1, Terms, a minor is “Any person, other than active duty military personnel, who has not attained the legal age of consent to treatments or procedures involved in the investigation. This age is determined under the applicable law of the jurisdiction in which the investigation is to be conducted.” Since cadets are considered active duty personnel when they take the oath of office at the beginning of their cadet career, cadets are considered emancipated minors and are allowed to be treated as adults in all Academy activities, to include human subject research. Colorado law supports this conclusion as well. As with all cadets, it is the policy of the USAFA IRB that cadets under age 18 may only participate in minimal risk research. The IRB may further limit their participation to social science research surveys that are (1) much less than minimal risk; (2) would cause little embarrassment/discomfiture during completion of the survey; and (3) would cause little embarrassment/discomfiture even if the survey were accidentally disclosed. Researchers who are considering collecting data from candidates before they in-process to the Academy, are forewarned that the rules governing research on minors will apply for all USAFA candidates who are under the age of majority in the jurisdiction in which they reside. Normally, in these circumstances, the board will restrict researchers to collecting data only from those USAFA candidates who have already reached the age of majority.

2.7.19.3. **(Added-USAFA)** Payment of Cadets for Participation in Research: Cadets may receive money as part of a research project as long as (1) the funds are not from a DoD source; (2) the cadet subjects are not receiving course credit for their participation.

2.7.20. **(Added-USAFA)** Pilot Studies: The module “What is research?” in the CITI Training module clearly states that pilot studies, such as giving a survey instrument to a few subjects in order to refine the questions, meets the definition of research in 32 CFR 219.102(d) and therefore is subject to IRB oversight. Researchers considering running pilot studies should submit a protocol for the study to the IRB for review, using the appropriate template for their study (e.g. exempt or full board review). Researchers should clearly state that the study is a pilot study in explaining the design of the research, particularly the sample size.

2.8. Medical Monitor. At the discretion of the IRB:

- 2.8.1. Serves as the subject advocate and ombudsman.
- 2.8.2. Discusses research progress with the principal investigator.

- 2.8.3. Coordinates and reviews adverse events with the principal investigator.
- 2.8.4. Interviews and consults on individual cases and reports to the IRB/PI any discrepancies or problems.
- 2.8.5. May stop a research study in progress, remove individual subjects from a study, or take whatever steps are necessary to protect the safety and well being of research subjects.
- 2.8.6. For Cooperative Oncology Group studies, a medical monitor is not needed if a data safety monitoring board is overseeing the study. For FDA regulated studies the sponsor appointed monitor may satisfy this requirement.

Chapter 3

RESEARCH IN AIR FORCE INSTITUTIONS

3.1. Assurances. All human research conducted or supported by the Air Force shall be conducted under an Assurance of compliance acceptable to the Air Force, unless the research is exempt from these regulations under 32 CFR 219.101(b). See 32 CFR 219.103(a). A DoD Assurance is required for research performed at DoD facilities and funded by the DoD. A DoD Assurance issued by the Air Force is required for research conducted by the Air Force at an Air Force facility. Any changes to an Assurance covering research conducted or supported by the Air Force must be prospectively approved by AFMSA/SGRC.

3.1.1. DoD Assurances issued by the Air Force. Applications for DoD Assurances issued by the Air Force must be reviewed and approved by AFMSA/SGRC prior to initiation of any human research. Completed applications must be forwarded to AFMSA/SGRC with policies and procedures for local IRB operation, including those governing continuing review of the research. All IRBs designated in DoD Assurances issued by the Air Force must be registered with AFMSA/SGRC along with an IRB membership roster. AFMSA/SGRC shall issue every Assurance a tracking number. The Air Force issues two types of Assurances: the Multiple Project Assurance (MPA) and the Single Project Assurance (SPA).

3.1.1.1. DELETED.

3.1.2. SPA

3.1.2.1. An SPA applies to only one project. Documentation of IRB review and approval of the covered study must be submitted to AFMSA/SGR along with the SPA application. SPAs are awarded for up to three years, subject to continuing review. A SPA institution that has demonstrated compliance with Assurance requirements may submit application for a MPA.

3.1.2.2. SPA for an Institution Utilizing Another Air Force Institution's IRB. When an institution such as a small clinic does not have an IRB, before conducting human research supported or conducted by the Air Force, it must obtain both a valid DoD Assurance issued by the Air Force and review and approval from a regional Air Force IRB.

3.1.2.3. International Assurance. All research taking place outside of the U.S. and conducted or supported by the Air Force must be conducted under an International Assurance acceptable to AFMSA/SGRC as per paragraph **3.1.4.1** Research conducted at Air Force facilities outside of the U.S. must be conducted under a DoD International SPA issued by the Air Force through AFMSA/AGRC. Due to legal, ethical, and cultural differences between the U.S. and the foreign country in which the research will take place, IRBs, AFMSA/SGRC, and investigators are instructed to take extra care in reviewing, approving, and conducting international research to ensure compliance with the spirit of ethical guidelines for the protection of human research subjects, as well as the letter of the law. See paragraph **3.2.5** of this instruction for additional information on conducting research outside of the U.S.

3.1.3. MPA. An MPA can apply to one or more human research projects.

3.1.3.1. Submit requests for an MPA to AFMSA/SGRC. Requests must include a statement of principles and policies, documentation of IRB review and local policies for IRB operation.

3.1.4. Non-Air Force Assurances. In most cases, a DoD Assurance will be required. However, in some cases, AFMSA/SGRC may accept an Assurance issued by DHHS. Whenever the Air Force accepts an Assurance not issued by the Air Force, the institution must provide a separate written assurance that it will comply with requirements unique to the Air Force, including this instruction and all attachments, and that it will report to the Air Force continuing compliance and safety issues, such as continuing reviews, adverse events, and protocol deviations, in accordance with this instruction.

3.1.4.1. Copies of all non-Air Force Assurances submitted by Air Force institutions must be provided to AFMSA/SGRC in order to ensure proper coordination with the Assurance-granting agency and compliance with the requirements outlined in this instruction.

3.1.4.2. Federalwide Assurance (FWA). DHHS issues FWAs for research funded by DHHS. Institutions participating in NCI Clinical Trials Cooperative Group projects are required to obtain an FWA from DHHS because NCI is an institute within DHHS. Air Force Institutions needing a DHHS FWA should not check the box on the FWA electing to apply the FWA to all of its human research.

3.1.4.3. Cooperative Project Assurance (CPA). A CPA is an Assurance previously issued by DHHS for facilities involved in NCI's Clinical Trials Cooperative Group studies.

3.2. Requirements for Special Categories of Human Subjects. The use of human subjects in research in which there is an intervention or interaction with subjects is limited to persons who are fully informed and who voluntarily agree to participate in the study. If the subject is legally incompetent to give consent (as with infirmed, minors, or patients in an unconscious state) and the proposed measures are intended to benefit the subject, then consent may be obtained from a legal guardian on the subject's behalf. Research supported or conducted by the Department of Defense that affects the following vulnerable populations shall meet the additional protections of 45 CFR 46, Subparts B-D: fetuses, pregnant women, or human in vitro fertilization (Subpart B); prisoners (Subpart C); and minors (Subpart D).

3.2.1. Active Duty Personnel as Human Subjects. The investigator, in consultation with the subject, should determine whether participation in a study would affect the ability of the subject to mobilize for readiness, to perform duties, or to be available for duty. Normally, if their participation could affect their performance, they should not be considered as a subject.

3.2.1.1. Active duty personnel may receive financial compensation for participation as a subject of research, as long as DoD funds are not used for payment and off duty employment is authorized. (Reference 24 U.S.C. 30)

3.2.2. Minors as Research Subjects. Minors may be used as subjects only when the protocol is intended to be of benefit to the subject and satisfies one of the categories in **3.5.1** or **3.5.2** of this instruction. In both cases, the investigator must solicit the assent of the minor according to paragraph **3.5.3**, as well as the consent of one or both parents or guardian.

3.2.2.1. The investigation may present greater than minimal risk to minor subjects if the proposed procedures present a prospect of direct benefit to the individual subject, and if the IRB finds that:

3.2.2.1.1. The risk is justified by the anticipated benefit to the subject.

3.2.2.1.2. The relationship of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches.

3.2.2.2. In some cases, minor subjects may be mature enough to understand the nature and consequences of their participation, or nonparticipation, in the study. The IRB must ensure that in these cases the investigators solicit the minor's consent, as well as the parent or guardian's, before performing a medical procedure. The investigator should assess the age, maturity, psychological state, and mental capacity of the minor subjects potentially involved in a study to determine if their consent has legal merit. Consult the legal advisor where a minor subject's capability to assent is in question.

3.2.3. Mentally Disabled Persons as Human Subjects:

3.2.3.1. A mentally disabled or institutionalized mentally infirm person may not participate as a test subject, unless the study would be impossible or meaningless if such subjects were excluded. The investigator may not use any such person as a test subject purely for the sake of convenience.

3.2.3.2. A mentally disabled or institutionalized mentally infirm person may not participate as a test subject unless:

3.2.3.2.1. The subject has given legally effective consent, or the subject's legal guardian has given effective third part consent, according to local law.

3.2.3.2.2. The proposed study is concerned with one or more of the following:

3.2.3.2.3. The diagnosis, treatment, prevention, or etiology of a particular impairment that inflicts the subject.

3.2.3.3. Any other condition from which the subject is suffering, provided there is a direct potential benefit to the subject, and prior testing has proved the risk to be acceptable.

3.2.3.4. The effect of institutional life on the institutionalized mentally infirm subject, and involves no appreciable risk to the subject.

3.2.3.5. Information which cannot be obtained from any other class of subjects.

3.2.3.6. If the mentally disabled or institutionalized mentally infirm person appears to have sufficient mental capability to comprehend what is proposed and is able to express his or her willingness to participate, the investigator should obtain consent.

3.2.4. Prisoners as Human Subjects. A prisoner may not participate as a human subject unless the proposed protocol is concerned with the diagnosis, treatment, prevention, or etiology of a particular impairment that afflicts the prisoner and unless the prisoner may derive a direct potential benefit.

3.2.4.1. Prisoners of War. The use of prisoners of war as research subjects is unequivocally prohibited. See DoD Directive 3216.2, paragraph 4.4.2.

3.2.5. Non-US Citizens as Human Subjects. In protocols conducted outside the United States involving non-US citizens as human subjects, the laws, customs, and practices of the country in which the study is conducted, or those required by this instruction, whichever are more stringent, shall take precedence. The study shall meet the same standards of ethics and safety that apply to studies conducted within the United States, involving US citizens.

3.2.6. Protocols Involving Biological or Chemical Warfare Agents. Research involving the use of human subjects for testing of chemical or biological warfare agents or nuclear weapons effects is generally prohibited. See DoDD 3216.2, paragraph 4.4.5., and 50 USC 1520a. Such research must be submitted to OUSDAT for approval prior to implementation.

3.3. Compensation for Human Subject Participation.

3.3.1. Active duty personnel may receive financial compensation for participation as a subject of research, as long as DoD funds are not used for payment and off duty employment is authorized. (Reference 24 U.S.C. 30)

3.3.2. In accordance with DoDD 6000.8, retired military personnel, dependents, and others not active duty that participate as subjects may be compensated when appropriate. When retired military personnel, dependents, and others not on active duty participate without compensation, records must document the subject's acknowledgement and agreement to participate without compensation for serving as subjects. Due to the possibility of injuries arising from participation in research greater than minimal risk research projects shall include an arrangement for treatment of any related injuries. Such arrangement may be that all subjects are eligible DoD healthcare beneficiaries, that are granted Secretarial Designation as DoD healthcare beneficiaries under applicable service regulations, or that specific obligations for such treatment have otherwise been undertaken. In no case shall any research request permit volunteers to sign a statement that purports to limit any right of a subject to compensation for possible injuries arising from participation in the research.

3.3.3. Retired military personnel, dependents, and others routinely entitled to medical care in military medical treatment facilities may participate as human subjects. Such persons may receive compensation for these services as authorized by applicable directives (B-158690, 45 Comptroller General 649, April 26, 1966).

3.3.4. Private citizens. U.S. Policy is to not accept voluntary services without compensation when such services may provide a basis for a future claim against the government. Individuals may enter into an independent contractor relationship with the Air Force and participate for compensation as authorized by applicable directives (45 Comptroller General 649).

3.4. Survey Research.

3.4.1. The investigator must contact the local IRB prior to initiating a research activity involving survey instruments or methods. The IRB will determine if the research (1) is exempt from further review or (2) the study presents minimal risk and is eligible for expedited review; or if (3) the study requires full board review. Exemption and expedited review categories are listed in 32 CFR 219. If a local IRB does not exist or if the survey will be used at multiple sites, then a regional IRB or AFMOA/SGOT may determine if the research is exempt.

3.4.2. Surveys which collect data through intervention or interaction with the subject or surveys which contain identifiable private information are not exempt and require IRB approval and informed consent.

3.4.3. Attitude and opinion surveys must be conducted IAW AFI 36-2601, Air Force Personnel Survey Program, February 1, 1996. Surveys within the Air Force at more than one base are to be approved by HQ AFPC/DPSAS, Randolph AFB, TX, IAW the Paperwork Reduction Act, Title 44, United States Code, Chapter 35. Any non-exempt survey conducted outside of the Air Force requires Office of Management and Budget (OMB) approval IAW Chapter 35 of Public Law 96-551, Paperwork Reduction Act. For more information on surveys, see AFI 37-124, *The Information Collections and Reports Management Program; Controlling Internal, Public, and Interagency Air Force Information Collections*, Mar 29, 1994.

3.5. Informed Consent Requirements.

3.5.1. Federal Statutory Limitations. 10 U.S.C. 980, limits the use of subjects in DoD or DoD-supported research to persons who are fully informed and who voluntarily agree to participate in the study. If the subject is legally incompetent to give consent (as with infirmed, minors, or subjects in an unconscious state) and the proposed measures are intended to benefit the subject, then consent may be obtained from a legal guardian on the subject's behalf.

3.5.2. When a consent form is required, the subject must sign the consent form in the presence of at least one witness, who attests to the subject's consent and attests to the subject's signature by signing in the place provided. ([Attachment 4](#)). Assent of a minor must be obtained when appropriate.

3.5.3. A written legal review of the Informed Consent Document must be obtained ([Attachment 10](#)) prior to IRB approval.

3.5.4. Retain copies of the IRB approved consent documents and legal review in the protocol records. Provide a copy of the consent document to the subject.

3.6. SG Approval of Research Protocols.

3.6.1. The SGROC must review and approve all greater than minimal risk protocols prior to initiation except as noted in [3.6.2](#) below. Protocols that are determined by the IRB to be no more than minimal risk to the subject must be sent to AFMSA/SGRC, which shall conduct audits in order to ensure compliance. Minimal risk studies may begin upon local IRB and Commander/AIO approval. Protocols that are determined to be exempt by the IRB Chair or designee must be evaluated using written criteria, reported to AFMSA/SGRC, and documented in the IRB minutes and in section 8 of the OF 310. The exemption must be referenced using the appropriate CFR rule. The OF 310 must be kept on file for audit purposes. If the SGROC disagrees with the IRB's determination, the research study may be temporarily suspended until resolution. Guidance for document submission to the SGROC is included in this instruction ([Attachment 7](#)).

3.6.2. The investigator may enroll subjects into local IRB and MTF/CC approved cooperative oncology studies prior to submitting the protocols to AFMOA/SGOT and the SGROC.

3.6.3. Oversight of oncology protocols by AFMOA/ SGOT ends after the protocol is closed to new subject registration and all local subjects have completed treatment. Due to National Oncology study requirements local facilities may be required to keep these protocols open at their sites until subject follow-up is complete.

3.6.4. Emergency use protocols must be sent to AFMOA/SGOT with the MTF commander's approval and the IRB recommendations.

3.7. Classified Research Protocols.

3.7.1. IAW 32 CFR 219 section 125, the requirements for review and approval of classified human research studies add further protections as follows:

3.7.1.1. Classified research protocols must have full IRB review, and at least one non-governmental voting member with appropriate security clearance in attendance.

3.7.1.2. Investigators must inform the subjects that the research is classified, give a clear explanation of what classified means, and give sufficient information including classified information to allow the subject enough information to give meaningful informed consent. The requirement for informed consent must not be waived and the investigator must obtain signed consent. The subject will also be informed of the identity of the sponsoring institution. In cases of dispute, the IRB shall determine whether potential subjects need access to additional classified information in order for the subject to make a valid assessment of the risks and benefits of participation in the study.

3.7.1.3. Classified Research Protocols must be recommended for approval by the majority vote of the IRB and approved by the institutional official before being forwarded through AFMOA/SGOT to the Secretary of Defense for final approval.

3.7.1.4. Any IRB member who does not believe a specific classified project should be approved may appeal the IRB recommendation to the Secretary of Defense within 20 days after the IRB meeting. All appeals will be forwarded to the Office of the Air Force Surgeon General through AFMOA/SGOT.

3.8. Adverse Events.

3.8.1. Adverse events must be reported to the IRB in accordance with local IRB policy. Serious, expected or unexpected adverse events must also be forwarded to the MTF Commander or AIO. Serious, unexpected and related adverse events must be sent to AFMOA/SGOT as soon as possible, but within 15 working days of being notified of the adverse event. The IRB will review the incident to evaluate the effect of the adverse event on the risks of harm to other research subjects and determine if a change in procedures/consent document is warranted. The PI will report the AE using the FDA MedWatch Form 3500 or equivalent ([Attachment 5](#)) and submit the form to the IRB for review of the incident.

3.9. Scientific Misconduct.

3.9.1. Air Force institutions must ensure that research is conducted under the highest ethical standards. In support of this responsibility, every allegation of research misconduct shall be investigated. All allegations of research misconduct shall be investigated in an independent, unbiased, and equitable manner that minimizes disruption to research in process unless the research misconduct could result in a threat to public health or safety. Written institutional policy governing research misconduct must be established in accordance with the requirements of DoDI 3210.7 and submitted to AFMSA/SGRC.

3.9.1.1. Seriousness of the misconduct. The commander should determine if the misconduct was intentional or reckless; was an isolated event or part of a pattern; had significant impact on the research record; or had significant impact on other researchers or institutions.

3.9.1.2. Administrative Actions, including but not limited to, letters of reprimand; the imposition of special certification or assurance requirements to ensure compliance with applicable regulations or terms of an award; suspension or termination of an active award; or suspension and debarment in accordance with the government-wide rule on non-procurement suspension and debarment, Subpart 9.4 of the Federal Acquisition Regulation, current edition. In the event of disbarment or suspension, the information will be made publicly available through the List of Parties Excluded from Federal Procurement and Non-procurement Programs maintained by the U.S. General Services Administration.

3.9.1.3. All allegations of research misconduct occurring within an institution shall be referred to and investigated by the AIO; however, SGR may investigate the allegation if there is a determination that 1) the institution is unable to conduct a thorough and unbiased inquiry and/or investigation; 2) it is in the public interest for the parent command to conduct the inquiry and investigation; or 3) the allegation involves a small institution or an individual that cannot reasonably be expected to respond. SGR shall investigate allegations of research misconduct occurring outside of an Air Force institution.

Chapter 4

RESEARCH IN AIR FORCE SUPPORTED INSTITUTIONS

4.1. Contractor Studies. This section sets out procedures for contracted research involving the use of human subjects. An organization may not award a contract for research involving the use of human subjects until the requirements of this instruction have been fully met.

4.1.1. Commanders/ AIOs who approve contracts using human subjects must comply with the procedures in this instruction.

4.1.2. Each RDT&E organization must manage its contracts to ensure contractor compliance with 32 CFR 219 and this instruction.

4.1.2.1. The Air Force will not award any contract that involves the use of a human subject unless an IRB has reviewed and approved the proposed protocol. If the proposing institution does not have an IRB, they may either establish one or request the services of an Air Force IRB or AFMOA/SGOT.

4.1.3. An Air Force IRB or AFMOA/SGOT must approve all contractor protocols involving more than minimal risk and all classified protocols.

4.1.4. The Air Force will not award a contract involving a human subject to an individual unless he or she is affiliated with or sponsored by an organization that can, and does, assume responsibility for that subject.

4.1.5. Any organization applying for a contract to conduct research involving a human subject must provide a written assurance that it will abide by the policy for protection of human subjects as stated in this instruction. Written assurance may be provided to the sponsoring Air Force institution using Optional Form (OF) 310. If the organization currently has an approved multiple-project assurance on file with the Department of Health and Human Service (DHHS), as described in 32 CFR 219.103(a), the organization must annotate this on OF 310.

4.1.6. The contractor must ensure it has obtained all necessary clearances and permits and has properly coordinated with other agencies, whether federal, state, or local.

4.1.7. Contractors must notify the US Air Force contracting agency and obtain IRB approval of any changes to the protocol prior to implementation. Contractors must have written procedures for notifying the US Air Force contracting agency of any misadventure or unanticipated adverse medical event that coincides with or possibly results from using human subjects in a US Air Force-sponsored research protocol. Include all the information required in paragraph 2.7 of this instruction.

4.1.7.1. The contracting agency must notify AFMOA/SGOT of all reported contractor unanticipated deviations from the approved protocol and reports of serious unanticipated adverse events.

4.1.8. For protocols involving more than minimal risk, the contractor will submit to the sponsoring Air Force organization a copy of contractor records documenting protocol review, approval, conduct, subject consent, and results.

4.2. Collaborative Investigations with Non-Air Force Organizations.

- 4.2.1. Collaborative studies with non-Air Force federal agencies or civilian organizations that involve subjects at Air Force facilities must comply with this instruction.
- 4.2.2. Air Force personnel may act as investigators in studies conducted outside of Air Force facilities only if the commander/AIO decides it is in the best interest of the Air Force. If such studies involve human subjects, the sponsoring facility's IRB must review and approve the study according to Federal law and regulations.
- 4.2.3. Non-Air Force investigators wishing to use subjects at Air Force installations must adhere to the requirements outlined in this instruction.
- 4.2.4. In order to conduct research on an Air Force installation, the investigator must obtain written permission from the wing/base or hospital commander in accordance with local policy.
- 4.2.5. Collaborative studies with non-Air Force federal agencies or civilian organizations that use SGROC funds must comply with this instruction. Such studies must have an Air Force principal investigator or associate investigator when funded by the SGROC. The protocol must be reviewed by a military IRB, approved by the facility commander/AIO and reviewed by the SGROC as appropriate.

Chapter 5

BUDGETING AND FUNDING

5.1. AFMOA/SGOT.

5.1.1. Follows DoDD 6000.8 policy for the funding and administration of military Clinical Investigation Programs (CIP's) in medical treatment facilities, dental treatment facilities and the Uniformed Services University of the Health Sciences. DoDD 6000.8 defines policy concerning study grants, cooperative agreements, cooperative research and development agreements, receipt of gifts, clinical investigation study subjects, and the prohibition of obligating or expending CIP funds for any external medical research project unless the study has been approved after an external peer review process.

5.1.2. Provides funds to support approved research protocols that have unique supply, equipment, or service requirements. Funds will not be used to hire additional personnel, to pay for reprints, or for temporary duty travel unless explicitly approved by AFMOA/SGOT.

5.1.3. Approves waivers for required technical support to conduct a study. The investigator must justify the need for such services.

5.1.4. Maintains final disposition authority for all unexpended funds.

5.1.5. Requires notification when SG funded protocols are submitted for publication.

5.2. Reporting.

5.2.1. Organizations awarded MPA's by AFMOA/SGOT will provide AFMOA/SGOT an accounting report using the quarterly reporting format provided by SGROC. RCS: HAFMOA-SG(Q)0004.

5.2.2. Principal investigators of study projects awarded Healthy Communities Research Program funding will provide a technical and accounting report to AFMOA/SGOT annually.

Chapter 6

GIFTS/GRANTS

6.1. Gifts to the Air Force.

6.1.1. Commanders of Air Force medical treatment facilities may accept gifts of a value not greater than \$50,000 that require only a small expenditure to accept and maintain. Reference AFI 51-601, *Gifts to the Air Force*.

6.1.2. Only the Secretary of the Air Force may accept a gift offer with a value over \$50,000. Send the signed letter from the donor offering the gift and the protocol through an Air Force IRB and the local commander to AFMOA/SGOT.

6.1.3. Federal law allows gifts to be accepted for use with MTF operations. To avoid the appearance of impropriety or violation of law, all gifts and benefits, offered in connection with research protocols must be fully disclosed and accepted according to AFI 51-601. Travel benefits may be accepted under the authority of *Title 31, United States Code*, Section 1353, when offered from a non-Federal source in connection with attendance on an official capacity at meetings or similar functions. Procedures for accepting travel benefits are found in Chapter 4 of the *Standards of Conduct*, DoD 5500.7-R, rather than AFI 51-601.

6.1.4. Gifts accepted in connection with the conduct of a particular Air Force protocol, may be delayed or terminated if necessary in the interest of meeting Air Force mission requirements.

6.1.5. The Air Force policy prohibits soliciting gifts, but does not prohibit researchers from applying for standard grants. However, the terms of any such grant applications must be consistent with the policies of AFI 51-601.

6.1.6. Gifts may be rejected under circumstances described in AFI 51-601.

6.1.7. If the donor is a defense contractor or subcontractor, the donor must state that the cost of the gift will not be charged either directly or indirectly, as an element of cost in any US Government contract.

6.1.8. The officer in charge of the MTF CI facility, or other officer designated by the commander will administer gifts received in connection with Air Force research protocols. Prospective donors should contact this officer for guidance on proper procedures for making gift offers. To avoid an actual or apparent conflict of interest, principal or associate investigators, or others directly involved in a research protocol, must not directly accept or administer gift funds accepted from the donor for use in connection with the clinical investigation.

6.2. Gift Procedures.

6.2.1. The donor or legal guardian must sign gift offers. All gift offers with a value over \$50,000 must be forwarded through the local commander to AFMOA/SGOT for submission to the Secretary of the Air Force.

6.2.2. Once the gift is accepted, the MTF/CC must ensure that proper actions are taken to receive and establish accounting for the gift according to the procedures in AFI 51-601.

6.2.3. Donors may give a wide variety of administrative, technical, or professional services to the Air Force as “Gifts of Service,” in support of a protocol or program and at no cost to the government.

6.2.4. The Office of the General Counsel has determined that the gift statute (10 U.S.C. 2601) and AFI 51-601 do not cover services, as provided by civilian employees or agents of nonfederal organizations, such as national cancer study groups.

6.2.4.1. When an offer of a gift of services in support of a research protocol is made, document the offer and terms of acceptance in a Memorandum of Understanding (MOU), using the example at [Attachment 9](#). The legal office servicing the MTF must review the MOU, prior to signature by the MTF commander and the donor, and prior to the donor’s providing any technical services.

6.2.4.2. The MTF must ensure that the donor has adequate liability insurance coverage for such personnel (*Federal Acquisition Regulation* 84-42, subpart 37.4; *Non-Personal Health Care Services*), and ensure compliance with existing Air Force policies relating to licensure, credentials review, and clinical privileges delineation as required by AFI 44-119, *Medical Service Clinical Quality Management*, Oct 1, 1995.

6.2.5. To avoid any appearance of a conflict of interest or violation of supplemental income rules, Air Force medical personnel assigned to or employed at the MTF and conducting the research protocol under this instruction may not engage in off-duty employment, or otherwise be compensated by non-Air Force sources, in connection with their work on such clinical investigations.

6.3. National Institutes of Health (NIH) Grants.

6.3.1. Application Procedures: Investigators may apply for NIH grants. NIH grants may require Office of the Secretary of the Air Force approval before submittal. Send application, along with the locally approved investigative protocol, including attachments, to AFMOA/SGOT for coordination. AFMOA/SGOT sends the protocol and application to the Secretary of the Air Force for approval.

6.3.2. Types of NIH Funding.

6.3.2.1. Direct Funding. If funds are awarded, establish specific accounting criteria for audit trails at the local institution.

6.3.2.2. Indirect Funding. Air Force institutions that have collaborative arrangements with other institutions such as national cancer groups or medical and dental schools, may receive the benefits of NIH funds awarded to the parent institution. In those cases where the parent institution receives and controls funds, the Air Force facility participating in the study may receive support. This indirect funding mechanism does not require Office of the Secretary of the Air Force approval, as prescribed above, since NIH funding to the parent institution is not directly under Air Force management.

Chapter 7

PUBLICATIONS

7.1. Air Force Support.

7.1.1. Publication of papers resulting from research investigation projects in military and civilian professional journals is highly encouraged. Clearance of the manuscript for publication must be done through local policy of the performing institution and according to AFI 35-101, *Public Affairs Policies and Procedures*, Dec 1, 1999.

7.1.2. Report all publications to the approving IRB.

7.1.3. A copy of technical reports and/or publications should be filed with the Defense Technical Information Center.

7.2. Mandatory Volunteer Statement.

7.2.1. All printed papers, articles, and reports pertaining to the use of volunteers within the provisions of this instruction must contain the following statement; "The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and AFI 40-402."

7.3. (Added-USAF) Prescribed and Adopted Forms.

7.3.1. **Prescribed Forms.** No forms are prescribed.

7.3.2. **Adopted Forms.** AF Form 847, *Recommendation for Change of Publication*

PAUL K. CARLTON, JR., Lt General, USAF, MC
Surgeon General

(USAF)

TAMRA L. RANK, Colonel, USAF
Vice Superintendent

Attachment 1

GLOSSARY OF REFERENCES AND SUPPORTING INFORMATION

References

- Title 10, United States Code, Section 980, *Limitation on Use of Humans as Experimental Subjects*
- Title 10, United States Code, Section 2601, *General Gift Funds*
- Title 10, United States Code, Section 8013, *Secretary of the Air Force*
- Title 21, Code of Federal Regulations, Parts 300 to 499, *Drugs for Human Use*
- Title 24, United States Code, Section 30, *Payments to Donors of Blood for Persons Undergoing Treatment at Government Expense*
- Title 31, United States Code, Section 1353, *Acceptance of Travel and Related Expenses from Non-Federal Sources*
- Title 32, Code of Federal Regulations, Part 219, *Protection of Human Subjects*
- Title 44, United States Code, Chapter 35, *Coordination of Federal Information Policy*
- Title 45, Code of Federal Regulations, Part 46, *Protection of Human Subjects*
- DoD Directive 5500.7, *Standards of Conduct*
- DoD Directive 3216.2, *Protection of Human Subjects in DoD-Supported Research*
- DoD Directive 6000.8, *Funding and Administration of Clinical Investigation Programs*
- (Added-USAF)** AFMAN33-363, *Management of Records*
- AFPD 40-4, *Clinical Investigation and Human Use in Medical Research*
- AFI 35-101, *Public Affairs Policies and Procedures*
- AFI 36-2601, *Air Force Personnel Survey Program*
- AFI 37-124, *The Information Collections and Reports Management Program; Controlling Internal, Public, and Interagency Air Force Information Collections*
- AFI 37-138, *Records Disposition Procedures and Responsibilities*
- AFJI 40-401, *The Use of Animals in DoD Programs*
- AFI 44-119, *Medical Services Clinical Quality Management*
- AFI 48-112, *Hyperbaric Chamber Program*
- AFI 51-601, *Gifts to the Air Force*
- AFMAN 37-139, *Records Disposition Schedule*
- Federal Acquisition Regulation*, current edition

Abbreviations and Acronyms

AETC—Air Education and Training Command

AFI—Air Force Instruction

AFMAN—Air Force Manual

AFMC—Air Force Material Command

AFMLO—Air Force Medical Logistic Office

AFMOA—Air Force Medical Operations Agency

AFMOA/SGOT—Clinical and Biomedical, Research and Development Division

(Added-USAFA) AFMSA/SGEC— The Surgeon General's Research Oversight & Compliance Division

AFPD—Air Force Policy Directive

AIO—Authorized Institutional Official (RDT&E facilities)

AMC—Air Mobility Command

CFR—Code of Federal Regulation

CIF—Clinical Investigation Facilities

CIP—Clinical Investigation Program

(Added-USAFA) CITI— Collaborative Institutional Training Initiative

CPA—Cooperative Project Assurance

CPRP—Cooperative Protocol Research Program

(Added-USAFA) CV— Vice Superintendent

(Added-USAFA) CW— Commandant of Cadets

(Added-USAFA) DF— Dean of the Faculty

DHHS—Department of Health and Human Services

DEFAS—Defense Finance and Accounting Service

DoD—Department of Defense

FDA—Food and Drug Administration

FMP—Family Member Prefix

ICD—Informed Consent Document

IDE—Investigational Device Exemption

IND—Investigational New Drug

IRB—Institutional Review Board

MEMO—Medical Equipment Management Office

MTF—Medical Treatment Facility

MPA—Multiple Project Assurance

NDA—New Drug Application

NIH—National Institutes of Health

OPRR—Office of Protection for Research Risk

OUSDAT—Office of the Under Secretary of Defense for Acquisition and Technology

(Added-USAFA) RDS—Records Disposition Schedule

RDT&E—Research, Development, Test and Evaluation

RSC—Radiation Safety Committee

SGROC—Surgeon General’s Research Oversight Committee

SPA—Single Project Assurance

SSN—Social Security Number

(Added-USAFA) USAFA—United States Air Force Academy

Terms

Adverse Event—Any untoward medical occurrence in a research or clinical investigations subject that is temporally related to the subject’s participation in a research protocol. An adverse event can be an unfavorable or unintended sign (including an abnormal laboratory finding), symptom, or disease. Adverse events may be further defined as either “serious” or “unexpected”.

Serious Adverse Event—Any untoward medical occurrence that results in

- a) **Death** – report all deaths (except National Cooperative Oncology studies, report fatal toxicity's.)
- b) **Life-threatening adverse experience** – report if the patient was at substantial risk of dying at the time of the adverse event or it is suspected that continued involvement in the research protocol (e.g., that the use or continued use of product under investigation would result in the patient’s death.) Examples: pacemaker failure; gastrointestinal hemorrhage; bone marrow suppression; infusion pump failure (except National Cancer Institute studies: report life threatening toxicities)
- c) **Inpatient hospitalization or prolongation of existing hospitalization** – report if admission to the hospital or prolongation of a hospital stay results because of an adverse event. Examples: anaphylaxis; bleeding causing or prolonging hospitalization.)
- d) **Persistent or significant disability/incapacity** – report if the adverse event resulted in a significant, persistent, or permanent change, impairment, damage or disruption in the patient’s body function/structure, physical activities or quality of life. Examples: CVA due to drug-induced hypercoagulability; toxicity; peripheral neuropathy.

or

- e) **Congenital anomaly/birth defect** – report if there are suspicions that exposure during the course of a research study (e.g., investigational drug/device) prior to conception or during pregnancy resulted in an adverse outcome in the child. Examples: malformation in the offspring cause by thalidomide.
- f) Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse experience when, based upon

appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Unexpected Adverse Event—Any untoward experience not identified in the protocol and or the consent form. For investigational drugs, unexpected is defined as any adverse drug experience that is not listed in the current investigators brochure. These include events that may be symptomatically and pathophysiologically related to an event listed in the labeling, but differ from the event because of greater severity or specificity.

Assent—A minor’s affirmative agreement to participate in a research investigation.

Associate Investigators—Members of the Air Force or other governmental agencies, and individuals at civilian universities, private institutions, or pharmaceutical companies who collaborate with the principal investigator.

Assurance of Compliance—A formal written, binding agreement that is submitted to a federal agency in which an institution promises to comply with applicable regulations governing research with human subjects and stipulates the procedures through which compliance will be achieved. The AF assurance is a signed agreement between the institution commander and AFMOA/SGOT which assures that all research will be performed according to the requirements of this instruction, 32 CFR 219 and 10 United States Code 980.

Authorized Institutional Official—Responsible for the oversight of research and IRB functions that has the legal authority to act and speak for the institution. This individual may be the commander or may be delegated to the director of research and development or flight commander. Selection of appropriate personnel will assure the protection of the rights and welfare not only of research subjects, but also the institution itself.

Behavioral Research—Human behavioral research is the application of the scientific method to the study of physical and mental processes as they occur in individuals or groups in specific instances or across the life span.

Biomedical Research—This includes both studies designed primarily to increase the scientific base of information about: (1) normal or abnormal physiology and development and (2) studies primarily intended to evaluate the safety, effectiveness or usefulness of a medical product, procedure, intervention.

Certification—The official notification by the institution to the supporting department or agency, in accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

Classified Human Research—Research involving “classified national security information” as defined in Executive Order 12958, sec. 1.1 (3 CFR, 1995 Comp., p. 333). The following definitions preceded by an * fall under the classified human research definition.

***Classified National Security Information**—(hereinafter “classified information”)--Information that has been determined pursuant to Executive Order 12958 or any predecessor order to require protection against unauthorized disclosure and is marked to indicate its classified status when in documentary form.

***Control**—The authority of the agency that originates information, or its successor in function, to regulate access to the information.

***Information**—Any knowledge that can be communicated or documentary material, regardless of its physical form or characteristics, that is owned by, produced by or for, or is under the control of the United States Government.

Composition of Institutional Review Board—The nonaffiliated member shall not be an employee or officer of the Federal Government (other than for purposes of membership on the IRB) and shall be required to obtain any necessary security clearances.

***Informed Consent**—For classified research only:

- (i) a disclosure that the project involves classified research and information sufficient to explain the nature of the classified research; and
 - (ii) a disclosure of the identity of the sponsoring agency, unless the head of the sponsoring agency makes a written determination, after consultation with the Director of Central Intelligence and the Assistant to the President for National Security Affairs, that providing this information could compromise intelligence sources or methods and, after consultation with the Director of the White House Office of Science and Technology Policy (OSTP) makes a written determination that the research involves no more than minimal risk to subjects.
- (2) An IRB may require disclosure to the subjects of the research any classified information that the IRB determines is necessary for the subjects to provide a valid informed consent.
- (3) An IRB may not approve a consent procedure which alters or omits any of the consent requirements in §.116 and may not waive the requirement that the investigator obtain informed consent and a signed consent form for any classified research.

***Expedited Review**—An IRB shall not allow use of the expedited review process.

***Approval by Agency Head**—Within 30 days of IRB approval of a classified research project that has not been appealed under paragraph (g) of this section, the head of the Department or Agency sponsoring the classified research (e.g. Secretary of Defense), and not the Agency head's designee or delegate, shall review and issue a written approval or disapproval of that project.

***Appeals from IRB Approvals of Classified Research**—Any IRB approval of a classified research project shall be subject to appeal by an individual member or members of the IRB.

(1) Appeals of any IRB approval shall initially be submitted to the head of the Department or Agency (e.g. Secretary of Defense) sponsoring the classified research within 20 days of the IRB approval. The Department or Agency head must render a written decision within 60 days of the date the appeal is submitted. The decision of the Department or Agency head may affirm the IRB approval, reverse the IRB approval, or remand the matter for further clarification from the IRB.

(2) The IRB member or members may appeal a decision of the head of the Department or Agency (e.g. Secretary of Defense) sponsoring the classified research that upholds the IRB approval to the Director of OSTP who shall review the IRB's decision and the decision of the head of the Department or Agency sponsoring classified research and approve or disapprove the project, or, at the Director's discretion, convene an IRB made up of individuals who are not employees or officers of the Federal Government (other than for purposes of membership on the IRB) each with the appropriate security clearances, to recommend approval or disapproval of the project. The Director of OSTP must issue a written decision on the appeal within 60 days of the date the appeal is submitted.

***Reporting Requirements**—The head of each Department or Agency sponsoring classified research (e.g. DDR&E) within the previous 12-month period shall, no later than September 30th of each year, report to the Director of OSTP the number of ongoing classified research projects involving human subjects and the number of classified research projects completed in the previous 12-month period. Each report required by this paragraph shall include the number of human subjects in each project and shall include information accurate as of the date the report is filed.

***Recordkeeping Requirements**—The head of each Department or Agency sponsoring classified research shall maintain permanent records of the deliberations of the IRB and the consent documents as well as any other related documents generated in connection with the decision to approve or disapprove a classified research project involving human subjects. (Information will be saved at the IRB level and AFMOA/SGOT level)

***Responsibilities of OSTP**—The Director of OSTP shall report the total number of classified research projects and participating subjects to the President and shall then report to the congressional armed services and intelligence committees and further shall publish the numbers in the Federal Register.

Clinical Investigation—A systematic investigation or study designed to develop or contribute to generalizable knowledge that is performed by, or together with, medical service personnel, usually in medical service facilities. The term does not include individual or group training of military personnel, such as combat readiness, effectiveness, proficiency, or fitness exercises.

Continuing Review—A periodic review of a research protocol by the IRB. The review must be substantive and meaningful, i.e., IRB members should receive and review a protocol summary and a status report on the progress of the research including (1) the number of subjects accrued; (2) a description of adverse events or unanticipated problems involving risks to subjects, withdrawal of subjects; (3) and a summary of any recent literature or findings, amendments or modifications of the research since the last review, especially information about adverse events associated with the research. Continuing review must occur at least intervals that are appropriate to the degree of risk, but not more than 365 days from the date of the previous IRB review. If the protocol was initially evaluated by a full IRB it must continue to undergo full board approval for any subsequent continuing reviews.

Cooperative Project Assurance—A streamlined assurance document developed to minimize effort in administering assurances for diverse Cooperative Protocol Research Programs (CPRPs). This Assurance is issued by the Office for Protection for Research Risks.

Cooperative Protocol Research Program—Are community-based, multi-center and multi-protocol in nature. This design brings the research to the subjects by dividing protocols widely and pooling resultant data to hasten conclusions and publication findings. All CPRP protocols undergo central review by the sponsoring DHHS agency (or sometimes by OPRR on the agency's behalf) prior to the release by the CPRP coordinating center for use by collaborating accrual sites.

Department of Health and Human Services (DHHS)—The U.S. Government's principal agency (executive branch) for protecting the health of Americans and providing essential human services. DHHS is comprised of operating divisions (1) the Public Health Service Divisions (including the Food and Drug Administration, the National Institutes of Health, Centers for Disease Control, Indian Health Service) and (2) Human Services Divisions.

Deviation—A one time departure from the IRB approved research protocol.

Devices—Medical devices are regulated by the Food and Drug Administration. FDA has established procedures for obtaining an "Investigational Device Exemption" (IDE) which applies to investigations conducted to determine the safety and effectiveness of medical devices.

The IDE regulations, 21 CFR 812, distinguish between Significant Risk (SR) devices and Non-Significant Risk (NSR) devices. Use of either kind of device in research requires IRB approval and use of informed consent.

Significant risk devices are those which present a potential for serious risk to the health, safety, or welfare of subjects, and are subject to FDA control and approval. To obtain FDA approval, the IRB must first review and approve; then the sponsor, i.e., the person or firm which initiates the investigation, submits an application for an IDE to the FDA. Examples of significant risk devices are implants and life-supporting equipment.

Non-significant risk devices include such items as crutches, elastic knee braces, bed boards, bedpans, medical chairs, and tongue depressors. In order to obtain approval to use a non-significant risk device, the investigator must submit a protocol to the IRB. The IRB must then determine the risk of the device.

Drugs—The Food and Drug Administration regulates the use of Investigational New Drugs (IND) (21 Code of Federal Regulations 50, 56, 312, and 314. An IND is defined as a new antibiotic, biologic or drug permitted by FDA to be tested in humans but not yet determined to be safe and effective for use in the general population and not yet licensed for marketing. FDA considers any clinical investigation involving an IND(s) to pose greater than minimal risks to subject; and, therefore requires full IRB review.

Emergency Use of Investigational Drugs or Devices—Emergency use of investigational drugs or devices on a human subject may be deemed necessary in a life-threatening situation. Emergency use is only for cases in which no standard acceptable treatment is available, and in which there is not enough time to obtain normal protocol approval.

Exempt Research Activities—Research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt:

(1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or

(ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:

(i) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and

(ii) Any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

(3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior is not exempt under paragraph 32 CFR 219.101 (b)(2), if:

(i) The human subjects are elected or appointed public officials or candidates for public office; or

(ii) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

(4) Research, involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

Expedited Review—Review of proposed research by the IRB chair or a designated voting member or group of voting members rather than by the entire IRB. Federal rules permit expedited review of certain kinds of research involving no more than minimal risk and for minor changes in approved research.

Full Board Review—Review of proposed research at a convened meeting at which a majority of the membership of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. For research to be approved, it must receive the approval of a majority of those members present at the meeting. Convened meetings may be conducted via telephone conference call providing each IRB member has received all pertinent material prior to the meeting, and each member can actively and equally participate in the discussion of the protocol. Minutes must clearly document that these two conditions have been met.

Human Subject—A living individual about whom an investigator (whether professional or student) conducting research obtains

(1) Data through intervention or interaction with the individual, or

(2) Identifiable private information.

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. "Private information" includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

Informed Consent—A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents thereof from liability for negligence.

Informed Consent Document (ICD)—A written consent document approved by the IRB. This document enables the investigator to obtain the legally effective consent of the subject or the subject's legal guardian. The ICD provides the prospective subject or the subject's representative with sufficient information to decide whether to participate in the proposed study.

Informed Consent Process—The informed consent process is intended to give a subject all the information that an individual reasonably would want about a study; to ensure that the subject understands this information; and to give the subject an opportunity to agree or decline to participate in the study. The process provides for interaction between the investigator and the subject.

Institution—Any public or private entity or agency (including federal, state, and other agencies).

Interaction—Communication or interpersonal contact between investigator and subject

Intervention—Physical procedures by which data are gathered (for example venipuncture) and manipulation of the subject or the subject's environment that are performed for research purposes.

Institutional Review Board (IRB)—A specially constituted review body established or designed by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research.

IRB Approval—The determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and federal requirements. This is required prior to AIO approval of research activities.

Institutionalized Mentally Infirm Person—Any person who is confined, whether by court order, voluntary commitment, or otherwise, in an institution for the care of the mentally ill, the retarded, the emotionally disturbed, the psychotic, or the senile, and others with impairments of similar nature, regardless of whether or not such person has been determined to be legally incompetent and regardless of whether or not he or she is capable of giving legally effective consent.

Investigational Drugs or Devices—Drugs or devices which are not FDA-approved for marketing. These include drugs or devices for which the FDA has provided either a notice of exemption as an Investigational New Drug (IND), or an Investigational Device Exemption (IDE), as appropriate.

Legally Authorized Representative—An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

Life Threatening—A situation where delay of immediate treatment would result in loss of life or serious bodily injury to the subject.

Medical Misadventure—An unauthorized deviation from an approved research protocol that has the potential to cause or has brought about injury or loss of life to a study subject. May be the result of human error or intentional alteration of the study procedures.

Medical Monitor—For any research involving human subjects an independent medical monitor may be appointed by name if the IRB determines that the research risk is greater than minimal. Medical monitors will be independent of the investigative team. Possess sufficient educational and professional experience i.e., physicians, dentists, psychologists, or other health care providers and be capable of overseeing the progress of the research protocol, especially issues of individual subject management and safety.

Mentally Disabled Person—Any person who, due to mental illness, mental retardation, emotional disturbance, psychosis, senility, or other impairment of a similar nature, is not capable of giving legally effective informed consent.

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

Minor—Any person, other than active duty military personnel, who has not attained the legal age of consent to treatments or procedures involved in the investigation. This age is determined under the applicable law of the jurisdiction in which the investigation is to be conducted.

Multiple Project Assurance (MPA)—A Multiple Project Assurance (MPA) is a document to assure compliance of an institution with federal regulations on protection of human research subjects. The Office for Protections from Research Risks (OPRR) is responsible for issuing MPA's for DHHS supported research. The issuing agency for the Air Force assurances is AFMOA/SGOT.

(Added-USAFA) Office of Primary Responsibility—Any headquarters, agency, or activity having primary functional interest in, and responsibility for a specific action, project, plan, or program.

Office of Protection from Research Risks (OPRR)—Responsible agency for developing and implementing policies, procedures, and regulations to protect human and animal subjects involved in research sponsored by the DHHS.

(Added-USAF) Policy—Statement of important, corporate-level direction which guides Air Force decisions. It is enforceable, and compliance with it is measurable. Policy is the framework connecting the abstract ideas or principles contained in vision, mission, and purpose statements to the specific and concrete statements of plans, goals, and objectives. Policy can be viewed as establishing bounds within which the organization will operate. Policy provides both a focus for Air Force action and a guide for the behavior of the organization and its members.

Principal Investigator (PI)—A person responsible for the conduct of the research trial at a trial site. If a team of individuals conducts the research, the investigator is the responsible leader of the team and may be called the principal investigator. "Associate investigator" includes any other individual involved with the research protocol.

Prisoner—Any person who is involuntarily confined in a penal or correctional institution, whether the institution is for the confinement or rehabilitation of juvenile offenders, for persons charged with or convicted of civil or criminal offenses, or for other purposes.

Private Information—Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

Protocol—The written, formal design or plan of an experiment or research activity. In the context of this regulation, the plan submitted to the IRB for review and approval. Elements of a protocol are outlined in [Attachment 2](#).

Radiation Safety Office—Approves certain radioactive drugs for use in human research subjects that otherwise might require an IND or an approved New Drug Application (NDA). The radioactive drug may be used to obtain basic information regarding human physiology, pathophysiology, or biochemistry. The radioactive drug may not be used for immediate therapeutic, diagnostic, or similar purposes or to determine the safety and effectiveness of the drug in humans.

Regional IRB—IRBs that review investigational studies for institutions without an established IRB or Assurance within a specific region. Regional IRBs have the same responsibility to human subject protection as if the extrinsic research study was approved at the IRB's institution. Air Force Regional IRBs are: Wilford Hall Medical Center, Keesler Medical Center, David Grant Medical Center and Wright Patterson Medical Center. They are responsible agents to evaluate research for compliance with the CFR and DoD regulations.

Research—A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

Research subject to regulation—Are intended to encompass those research activities for which a federal department or agency has specific responsibility for regulating as a research activity, (for example, Investigational New Drug requirements administered by the Food and Drug Administration). It does not include research activities which are incidentally regulated by a federal department or agency solely as part of the department's or agency's broader responsibility to regulate certain types of activities whether research or non-research in nature (for example, Wage and Hour requirements administered by the Department of Labor).

Research Focus Area—A general category of military medicine in which a study's relevance may be described. The Research focus area of an investigative study may include any of the following five categories: Medical Readiness (MR), Prevention (Primary P-1, Secondary P-2, Tertiary P-3), Medical Utilization (MU), Managed Care (MC), or Treatment, Diagnosis or Other (TDO).

Scientific Misconduct—Fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. Fabrication is making up results and recording or reporting them. Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record. Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit, including those obtained through confidential review of others' research proposals and manuscripts. Research misconduct does not include honest error or honest differences of opinion. A finding of research misconduct requires that: there be a significant departure from accepted practices of the scientific community for maintaining the integrity of the research record; the misconduct be committed intentionally, or knowingly, or in reckless disregard of accepted practices; and the allegation be proven by a preponderance of evidence.

Single Project Assurance (SPA)—A written assurance that an institution will comply with federal regulations on protection of human research subjects. SPAs are limited in use and duration to a single research protocol. Institutions not holding a MPA with the Air Force AFMOA/SGOT office or the DHHS Office for Protections from Research Risks must negotiate a SPA with AFMOA/SGOT prior to initiation of the research protocol.

Subject Consent—Informed consent given by a prospective human subject who has the legal capacity to give such consent. For active duty military personnel participating in a US Air Force research investigation or collaborative study, there is no minimum age limitation. Consent must be given voluntarily, freely, and without any use of force, fraud, deceit, duress, constraint, coercion, or unlawful or improper inducement. The subject must possess sufficient understanding of the implications of his or her participation in the study in order to make an informed decision. A subject is free to withdraw participation at any time without jeopardizing his or her rights to treatment.

Surgeon General's Research Oversight Committee -(SGROC)—The SGROC meets quarterly to address issues related to protections of human subjects and animal research. SGROC members provide a comprehensive and expert second level review of research protocols initially approved by AF IRBs.

Surveys—Data collection, using personal or telephonic interviews, or self-administered questionnaires, etc. from a sample of ten or more persons, to elicit information. Examples of types of information include, attitudes, opinions, behavior, or demographic, social, or economic data, used for research and/or policy assessment. The key documents guiding survey requirements are DoD Instruction 1100.13 and AFI 36-2601. Surveys of attitudes and opinions of Air Force service members beyond the IRB's jurisdiction are subject to approval by HQ AFPC/DPSAS, Randolph AFB, TX (See AFI 36-2601)

Technical Assistants—Civilian employees or agents of nonfederal organizations, such as national cancer study groups, who provide to the Air Force, at no cost to the government, a wide variety of administrative, technical, or professional services in support of a research investigation protocol or program. The personnel rendering the services are not normally subject to the control and supervision of federal supervisors, which usually occurs in relationships between the government and its employees.

Third Party Consent—Consent given by the parents, legal guardian, or other legally authorized third party who represents the prospective human subject's welfare and interest. Third party consent may be used if the prospective human subject legally is not capable of giving consent. This third party consent is subject to all of the same criteria for full and complete disclosure as is the subject's own consent, and must be freely given.

Unanticipated Medical Event—An unforeseeable, unpreventable event that causes injury or loss of life to a study subject, after all the guidelines set forth in an approved clinical investigation protocol have been followed. An adverse drug reaction is an example of such an event.

Voluntary—Free of coercion, duress, or undue inducement. Used in the research context to refer to a subject's decision to participate (or continue to participate) in a research activity.

Attachment 2

SAMPLE PROTOCOL SUMMARY/ABSTRACT

The following sample format is intended to minimize effort towards future publication. If the work is likely to be published in another journal, use of that journal's format may be more appropriate.

Title: The summary or abstract should include the complete title of the article.

Authors: All authors should be cited in the format required for the journal in which you wish to publish. Include the institution where the authors are assigned.

Body of the Abstract: No information should be reported in the abstract that does not appear in the text of the manuscript. The information in the summary/abstract should contain no more than 250 words under the following headings: Context, Objective, Design, Setting, subjects (or participants), Interventions (only if there are any), Main Outcome Measure(s).

Context: The abstract should begin with a sentence or 2 explaining the (or other) importance of the study question.

Objective: A precise objective or study question addressed in the report **MUST** be stated (e.g. "To determine whether..."). If more than one objective is addressed, the main objective should be indicated and only key secondary objectives stated. If an a priori hypothesis was tested, it should be stated.

Design: The basic design of the study should be described. The number of years of the study and the duration of follow-up, if any, should be stated. As many of the following terms as apply should be used.

A. **For intervention studies:** Randomized controlled trial; nonrandomized controlled trial; double-blind; placebo controlled; crossover trial; before-after trial.

B. **For studies of screening and diagnostic tests:** Criterion standard (that is, a widely accepted standard with which a new or alternative test is being compared; this term is preferred to gold standard); blinded or masked comparison.

C. **For studies of prognosis:** Inception cohort (subjects assembled at a similar and early time in the course of the disorder and followed thereafter); cohort (subjects followed forward in time, but not necessarily from a common starting point); validation cohort or validation sample if the study involves the model of clinical predictions.

D. **For studies of causation or association:** Randomized controlled trial: cohort: case-control: survey (preferred to cross-sectional study).

E. **For descriptions of the features of medical disorders:** Survey; case series

F. **For studies that include a formal economic evaluation:** Cost-effective analysis; cost-utility analysis; cost benefit analysis. For new analyses of existing data sets, the data set should be named and the basic study design disclosed.

Setting: To determine the applicability of the report to their own research circumstances, the study setting(s) should be described.

Subjects or other Participants: The clinical disorders, important eligibility criteria, and key sociodemographic features of subjects should be stated. The numbers of participants and how they will be selected must be provided.

Intervention(s): The essential features of any interventions should be described, including their method and duration of administration.

Main Outcome Measure(s): The primary study outcome measurement(s) should be indicated as planned before data collection begins.

*Note: The information above has been adapted from The Journal of the American Medical Association (JAMA), July 7, 1999 - Vol 282, No.1 pp86-88.

Attachment 3

SAMPLE FORMAT, PROTOCOL FOR HUMAN RESEARCH

Use of this sample format is recommended. However, IRBs may modify the format to accommodate local needs. Investigators should contact their institute's protocol coordinator for specific format requirements.

1. Title of Investigation

2. Names/Office Symbol/Phone Extension/e-mail address of Principal Investigator, Associate Investigators, Collaborative Investigators, and Medical Monitor.

3. Facility and or Contractor. If this is a collaborative/multicenter study, identify the other participating facilities.

4. Purpose of Investigation. Give a brief summary, including hypothesis or question to be answered and the study relevance to the mission of the armed forces.

5. Risk / Category Of Study.

5.1. Risk: This research study is Exempt, Minimal Risk or Greater than Minimal Risk.

5.2. Category of Study: Medical Utilization (MU), Prevention (P), Medical Readiness (MR), or Treatment/ Diagnosis/ Other (TDO). For RDT&E studies, state the risk versus benefits of the study.

6. Technical Approach.

6.1. Summarize all information needed for an adequate evaluation. Include details of the experimental design, a description of methods to be used, and the number, age, and sex of subjects and controls. Essentials are experimental design, methodology and instrumentation, description of subjects and controls (number, age, sex, inclusion and exclusion criteria, and stop rules), data collection, and proposed analysis of the data collected.

6.2. For protocols involving human test subjects, describe risks, discomforts, and safeguards, as well as alternative available treatments.

6.3. Provide information on collaborative efforts with others engaged in similar research, such as medical and dental schools, drug companies, and national study groups. Collaborative protocols should clearly delineate the responsibilities between the various institutions or groups, as well as medical treatment facilities.

7. Investigation Schedule.

7.1. Date investigation will begin.

7.2. Duration.

7.3. Time phases.

7.4. Date of completion.

7.5. Factors which may adversely influence this schedule.

8. Experimental Subjects.

8.1. If experimental subjects are involved, include the following statement:

"All subjects will be treated in compliance with AFI 40-402, and applicable FDA and HHS guidelines."

8.2. Human Test Subjects. Specify the age range of the participants in the protocol. Include the age of minority under local law, if applicable. Include subject inclusion and exclusion criteria and schedule of subject evaluation studies to be performed before, during, and after completing the study.

9. Use of Investigational Drugs. If the investigation concerns human studies of treatment or diagnostic procedures involving the use of medications or radiopharmaceuticals not approved by the FDA, include the approved IND number and the following information about the investigational drug:

9.1. Chemical composition of the drug

9.2. Other names of drug

9.3. Side effects, from most common to rarest

9.4. Dosage rate schedule

9.5. Modifications in treatment, if side effects occur

9.6. Medications to be used or not used during the study

10. Use of Investigational Devices. If investigational devices are used on human subjects, provide the Investigational Device Exemption (IDE) number, a copy of the FDA letter assigning the IDE number or a copy of the manufacturer's letter approving the principal investigator or medical facility to perform the study under the auspices of their IDE number.

11. Support Required.

11.1. List all tests/tasks you would like performed and by whom to include Main Lab Support/or Radiology Support.

11.2. Pharmacy Support - List the drugs unfunded by the Surgeon General's Office or non-DoD source that will come from the Pharmacy budget. Indicate the quantity, storage and preparations.

11.3. Radioisotopes - If radioisotopes are to be used, describe here.

11.4. Data Analysis - Describe what data will be compared, and by what method. Consult with the Biostatistician for assistance.

11.5. Other Support - List a separate subparagraph for any other specific support required (e.g. nursing support, storage of specimens, support from other departments/services/flights). Indicate whether support is standard of care or beyond standard of care.

12. Equipment and Supplies. List items that the local research facility will need to purchase to accomplish the protocol. Do NOT include routinely stocked items that your department will provide.

13. Personnel Data.

- 13.1. Medical Facility Commander (name, grade, and title)
- 13.2. Investigator and Associate Investigators (name, grade, and title)
- 13.3. Medical Monitor (name, grade, and title)

14. Manpower. Estimate number of work hours to be applied to the investigation, categorized by Air Force Specialty Code (AFSC); for example:

- 14.1. 1 Captain, AFSC XXXX, __total hours duty time, __total hours off-duty time
- 14.2. 1 Staff Sergeant, AFSC 4A051, 30 Hours, 5 hours
- 14.3. 1 GS-5 Secretary, AFSC 4A051, 60 Hours, 0 hours

15. Bibliography. After a thorough review of the appropriate literature, list the major publications in the field of the investigation.

16. Attachments.

- 16.1. Sample Informed Consent Document (if applicable).
- 16.2. Curriculum vitae of investigators.
- 16.3. Protocol Summary (if required locally)
- 16.4. Other attachments if applicable, such as: IND/IDE supportive documents, contractor assurances, legal review of ICD, any other supportive documentation.

Attachment 4

SAMPLE FORMAT FOR INFORMED CONSENT DOCUMENT

Instructions are in italics.

_____ *or (text in parenthesis) indicates that the investigator should fill in the appropriate information.*

Model text is in regular font. Please write consent for 6-8 grade reading level.

INFORMED CONSENT DOCUMENT

(Name of Research Facility)

(Address)

(Base AFB, State, ZIP)

(IRB Approval Dates e.g. 22 Jan 00 - 21 Jan 01)

PRIVACY ISSUES: Records of my participation in this study may only be disclosed in accordance with federal law, including the including the Federal Privacy Act, 5 U.S.C. 552a, and its implementing regulations. I have read the Privacy Act Statement contained in DD Form 2005. I understand that records of this study may be inspected by the U.S. Food and Drug Administration (FDA), the sponsoring agency and/or their designee, if applicable.

TITLE OF STUDY

Place title here

INVESTIGATORS' NAMES, DEPARTMENTS, PHONE NUMBERS

List Investigator names here

PURPOSE OF STUDY

You are asked to consider participation in a research study at **(name of location)**, (sponsored by the _____ **(if pertinent)**), entitled "**(name of study)**".

The purpose of the study is _____.

This study will enroll *(approximate number)* of subjects over a period of *(number of days/months/years)*. You will be asked to make *(approximate number)* of *(inpatient/outpatient)* visits during your participation.

For studies involving the use of investigational drugs or devices, add the following:

This study involves use of an investigational _____ (*drug or device*) called _____ (*name of test article*). This means that the drug (or device). This means that the _____ (*drug/device*) has not yet been approved by the Food & Drug Administration (FDA) for _____ (*treating/preventing/diagnosing*) _____ (*disease or condition*). But the FDA has not objected to its use to study its safety and effectiveness.

For Phase I investigational drug studies, include a statement like this: This is an early human study to examine the safety of this drug. You are one of the first subjects to participate in the study.

For Phase II/III investigational drug studies, include a statement like this: The safety of this drug has been tested in (*number*) prior research subjects. This study will test if the drug is effective.

PROCEDURES

If you volunteer to participate in this study, we will ask you to do undergo the following procedures. ***Identify and describe the procedures using lay language, short sentences and short paragraphs. The use of table or flow diagrams will help to organize this section and increase readability. Distinguish which procedures are experimental and which are standard clinical treatments. Include screening evaluations and a listing of inclusion/exclusion criteria. State the frequency of tests, x-rays, etc.***

If blood will be drawn, explain the method and the amounts both in cc's and teaspoons or tablespoons. If blood will be collected for standard care, but in a greater volume for the study, explain that.

If a procedure such as a skin biopsy is to be done, explain the procedure from cleansing the skin, injection of a local anesthetic, to application of the bandage.

If a drug will be administered, state the name and type of drug, route of administration, duration of time and frequency of administration. Indicate if the drug is investigational or is being used outside its labeled indications.

For randomized studies, include a paragraph on randomization procedures. If appropriate, explain that there may be a change in treatment/procedures based on the subject's response, i.e., the subject may be assigned to a different treatment arm or removed from the protocol.

As a participant, you will be randomized to one of (*number*) groups described below. Randomized means that you are put into a group by a selection similar to flipping a coin. You will have an _____ (equal/one in two, one in three, etc.) chance of being assigned to any of the groups.

For placebo controlled studies

This study includes a placebo, which is an inactive, harmless substance that looks like the study medication. You will have a one in (*number*) chance of being in the placebo group.

For blinded studies, describe blinding in simple terms.

For single blind

This study is a single blind study. This means that you will not know whether you are receiving the study medication or the placebo.

For double blind

This study is a double blind study. This means that neither you nor your provider will know whether you are receiving the study medication or the placebo. In the event of an emergency, there is a way to determine what you are receiving.

Closing sentence for this segment

Should your physician find it necessary for you to have a procedure requiring additional informed consent, a separate informed consent document will be completed at the time of the procedure.

RISKS/INCONVENIENCES

Identify each procedure and describe any reasonably foreseeable risks, discomforts, or inconveniences. For example, state that they may experience bruising and soreness at the site where blood is drawn. Make some estimate of the frequency or severity of the risk, if known. If no risks are known, state “there are no known risks associated with this study.” In addition to physiological risks and discomforts, describe any psychological, social, or legal risks that might result from participation in the study.

If drugs are involved, the following information must be outlined below

The drug to be used in this study is (*name of drug*), also known as (*other names for the drug*). Possible side effects of the drug are (*list those the subject may observe, and those the investigator will watch for in laymen’s terms please. List other appropriate information*).

If the drug/procedure is potentially harmful to an embryo or fetus, add the following statement.

If you are pregnant or breast feeding, this treatment will not be offered. If it is possible that you may be pregnant, a pregnancy test will be done. If you are sexually active, you should take precautions to avoid the possibility of becoming pregnant or getting someone pregnant. You are advised to use an effective contraceptive method including abstinence, since it is not known how these drugs could affect an unborn child. If you become pregnant or feel you might be pregnant, contact your provider and the study investigator.

BENEFITS

The possible benefit of your participation is _____. ***Potential benefits to subjects or others should not be overstated. If there is no likelihood that participants will not benefit from participation in the study (e.g., a Phase I drug or centrifuge study) state so in clear terms.***

For studies requiring surrogate consent, e.g. pediatric volunteers, incompetent adults. Include this statement:

This research study is intended to benefit you. The potential benefit of this treatment would be *(describe, i.e.) (prolongation of disease control, prolongation of life, potential increase in the chances of curing disease. For research involving greater than minimal risks and enrolling minors, the study must present the prospect of direct benefit to an individual subject).*

Or, if appropriate: It is intended that the treatment on this study is an attempt to give you at least as good a chance of controlling your disease as standard treatments. However, there is no guarantee or promise that you will benefit from this study.

If appropriate: This study may also benefit others by helping to find out whether this treatment is better than the others in treating this disease.

ALTERNATIVES

If you decide not to participate in this study, other treatment, including _____ and/or _____ may be available to you.

OR

Choosing not to participate is an alternative to participating in this study.

EVENT OF INJURY

Use this paragraph standard in consent forms for active duty, dependent, retirees, or federal civilian employees.

Your entitlement to medical and dental care and/or compensation in the event of injury is governed by federal laws and regulations, and if you have questions about your rights or if you believe you have received a research-related injury, you may contact the Director of the Clinical Investigation Facility (or locally determined POC) at ***(phone number)***, the Customer Subject Representative at ***(phone number)***, the medical monitor or the investigator.

For protocols involving subjects who contracted employees of the federal government who are participating in the research outside the scope of their contracted employment use this statement:

Should you be injured as a direct result of being in this study, you will be provided medical care for that injury at no cost. You will not receive any compensation (payment) for injury. This is not a waiver or release of your rights. Medical care is limited to the care normally allowed for Department of Defense health care beneficiaries (patients eligible for care at military hospitals and clinics). Necessary medical care does not include in-home care or nursing home care. In case of any medical incident, you will be transported to ***(name of treatment facility)*** for care, unless personnel on site judge it to be an emergency, in which case they will call for ambulance service. If you have any questions, you may contact the medical monitor at ***(telephone number)*** Director of the Clinical Investigation Facility (or locally determined POC) at ***(phone number)***, the Customer Subject Representative at ***(phone number)***, or the investigator at ***(phone number)***.

OCCURRENCE OF UNANTICIPATED ADVERSE EVENT

(This paragraph standard in all consent forms) If an unanticipated event occurs during your participation in this study, you will be informed immediately. If you are not competent at the time to understand the nature of the event, such information will be brought to the attention of your next of kin.

CONFIDENTIALITY

Describe how personal identities will be protected: When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity. Complete confidentiality cannot be promised, particularly for military personnel, because information regarding your health may be required to be reported to appropriate medical or command authorities.

If the study involves the collection of photographs, videos, or audiotapes, describe how confidentiality of the subject will be maintained

When research records may be subject to inspection by FDA, funding agency or industrial sponsor:

The (name of agency, e.g., U.S. Food and Drug Administration (FDA), the sponsoring agency, and/or their designee) may inspect your study records.

DECISION TO PARTICIPATE

(This paragraph is recommended as standard for all consent forms.)

The decision to participate in this study is completely voluntary on your part. You may choose not to take part in the study. Dr. _____ will answer any questions you have about this study, your participation, and the procedures involved. Dr. _____ will be available to answer any questions concerning procedures throughout this study. If significant new findings develop during the course of this study that may relate to your decision to continue participation, you will be informed.

You may withdraw your consent at any time. *(As appropriate, describe withdrawal procedures.)*

Your decision will not affect your eligibility for care or any other benefits to which you are entitled.

If appropriate: If you decide to discontinue further participation in this study, you will continue to receive acceptable standard medical treatment for your condition. The investigator or primary physician may terminate my participation in this study at any time if he/she feels this to be in your best interest.

I have read all of the above. My questions have been answered concerning areas I did not understand. I am willing to take part in this study. After I sign this form, I will receive a copy.

(Subject's Printed Name)

(Subject's SSN)

()

*(Subject's Signature)

(FMP & Sponsor's SSN)

(Date & Time)

(*if the subject is a minor, it is recommended that both parents/guardians sign the ICD (if possible)

(Advising Investigator's Signature)

(Date)

(Witness's Signature)

(Date)

NOTE: If subjects who are minors may be involved, add the following statement: "If subject is a minor and in, the opinion of the attending physician, the minor can understand the nature and consequences of his or her participation in the study, the minor should be fully informed and indicate his/ her assent by signing this line. If such minor subject is physically unable to sign, the parent or guardian may sign for him or her as evidence of the minor's assent."

Attachment 5

SAMPLE FORMAT FOR SERIOUS OR UNEXPECTED ADVERSE EVENT REPORT

DATE

MEMORANDUM FOR (Office Symbol - Institutional Review Board)

FROM: (Your Office Symbol / Investigator(s) Name, Address)

SUBJECT: Serious or Unexpected Adverse Event

1. **Protocol Number:** (XXX-YYYY-NNNN)2. **Protocol Title:**3. **Type of Adverse Event:** (*Choose one below - Serious Adverse Event or Unexpected Adverse Event*)*Serious Adverse Event* (If reporting a Serious Adverse Event, choose one of the types listed below, delete others)a) **Death** – report all deaths (except National Cooperative Oncology studies, report fatal toxicity's.)b) **Life-threatening adverse experience** – report if the patient was at substantial risk of dying at the time of the adverse event or it is suspected that continued involvement in the research protocol (e.g., that the use or continued use of product under investigation would result in the patient's death.) Examples: pacemaker failure; gastrointestinal hemorrhage; bone marrow suppression; infusion pump failure (except National Cancer Institute studies: report life threatening toxicities)c) **Inpatient hospitalization or prolongation of existing hospitalization** – report if admission to the hospital or prolongation of a hospital stay results because of an adverse event. Examples: anaphylaxis; bleeding causing or prolonging hospitalization.)d) **Persistent or significant disability/incapacity** – report if the adverse event resulted in a significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities or quality of life. Examples: CVA due to drug-induced hypercoagulability; toxicity; peripheral neuropathy.e) **Congenital anomaly/birth defect** – report if there are suspicions that exposure during the course of a research study (e.g., investigational drug/device) prior to conception or during pregnancy resulted in an adverse outcome in the child. Examples: malformation in the offspring cause by thalidomide.f) Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse experience when, based upon appropriate medical judgment, they may **jeopardize the patient or subject** and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

OR

Unexpected Adverse Events - In general, an unexpected adverse event is any untoward experience not identified in the protocol and or the consent form. For investigational drugs, unexpected is defined as any adverse drug experience that is not listed in the current labeling for the drug product. These include events that may be symptomatically and pathophysiologically related to an event listed in the labeling, but differ from the event because of greater severity or specificity. The key to classifying adverse events is they are not listed in the current product label, in the Investigator's Brochure and not included in the risk description section of the current protocol and informed consent document. (National Cancer Institute studies: report previously unknown toxicity's)

Any adverse experience associated with the study that is both serious and unexpected must be reported to the IRB immediately (within 24 hours – even if all the information is not known). Summarize the serious, unexpected adverse event below. You must answer ALL the questions below for each AE)

- a) Date of AE
Type of Adverse Event
date (e.g. death, allergic reaction)
- b) Relationship of adverse event to the study: *(Choose only one.)*
Definitely Probably Possibly Unlikely Definitely Not
- c) If this is a multi-center study, does the AE involve a patient enrolled at this institution? *Y/N*
- d) Classify the severity of the AE: *(choose one: fatal, life-threatening, severe, moderate, mild)*
- e) Describe the adverse event. *(Include information on any medications or medical devices under investigation, route of administration, dosage, and reason for use, action taken regarding product use, clinical outcome. You may attach the safety report if this is an adverse event being reported by multi-center clinical trials)*

4. **Signature of Principal Investigator:** *(Please note that only the PI, may sign the adverse event report)*

5. **Signature of the IRB Chairman:**

Attachment 6**SAMPLE FORMAT FOR EMERGENCY TREATMENT REQUEST**

DATE

MEMORANDUM FOR (FLIGHT COMMANDER'S OFFICE SYMBOL)

Local Coordination

JA

SGO

SG

FROM: Your Office Symbol/Your Name

Your Facility's Name

Facility Address

SUBJECT: Emergency Treatment Request for (Protocol number and "title")

1. SUBJECT INFORMATION (Include the following)

Full name

Age

Patient's FMP/SSN

Sponsor's SSN

2. RESPONSIBLE PHYSICIAN(S) (Include the following)

Full Name

Rank,

Office Symbol

Phone number and beeper number

Whether your staff, resident or civilian and the facility name

3. INITIAL JUSTIFICATION FOR USE (Include the following)

Diagnosis

Proposed Emergency Treatment (What treatment is requested)

Risks (Include known/anticipated side effects of proposed therapy and patient's risk of this emergency therapy if not received).

Reason Standard Alternative treatment not used

4. THERAPEUTIC PLAN (Include the following)

Safeguards (Include follow-up measures that will be used to minimize risks of therapy)

Duration of planned study

Dose and frequency regimen (Include dose and frequency modification plan of side effects occur

5. NATURE OF DRUGS OR DEVICES (Include the following)

Trade and generic name

Name of manufacturer

Name of supplier

IND # for device

Name of the individual or manufacturer or supplier who holds the IND or IDE number.

6. CDC, NCI OR FDA COORDINATION (If the proposed therapy required consultation with the Centers of Disease Control (CDC), National Cancer Institute (NCI) or Food and Drug Administration (FDA), include the name, department, and phone number of the individual contacted. If none, enter N/A.

INVESTIGATOR

SIGNATURE BLOCK OF

Attachments:

1. Proposed ICD
2. Drug/Device Supplier Info

Approved/Disapproved

SIGNATURE BLOCK OF YOUR MEDICAL
GROUP COMMANDER OR DEPUTY

(The following paragraph is mandatory - type it verbatim at bottom of letter).

PRIVACY ACT STATEMENT

Authority: 5 USC 552a, AFI 33-332. Principle Purposes: To authorize emergency participation in approved clinical investigation protocol; to document justification for emergency treatment; and to define the therapeutic plan. Routine uses: To be placed in the investigational folder to document approval of the emergency use of an investigational drug or device. Information furnished may be disclosed to DoD officials/employees who need this information to perform their duties; to Federal, State and local medical authorities in appropriate cases; to sponsors of clinical trials in appropriate; and to the Centers for Disease Control (CDC), National Cancer Institute (NCI), or Food and Drug Administration (FDA). The social security number SSN is used for positive identification. Disclosure of SSN is voluntary.

Attachment 7

SAMPLE FORMAT FOR PROTOCOL SUBMISSION GUIDANCE

A7.1. AFMOA/SGOT. AFMOA/SGOT processes protocols for the SGROC. The following documents are needed for protocol approval consideration:

A7.1.1. **Protocol.** Submit one copy of the IRB approved protocol with all endorsements.

A7.1.2. **Protocol Amendments/Changes.** Submit one copy of the approved protocol amendment/change.

A7.1.3. **Protocol Summary.** Submit one copy of the IRB approved protocol summary with all endorsements.

A7.1.4. **Change in PI Memorandums.** Submit one copy of the Change in PI Memorandum endorse by the investigators involved.

A7.1.5. **Final Reports.** Submit one copy of the endorsed Final Report.

A7.1.6. **Informed Consent Document.** Submit one copy of the IRB approved ICD. Submit additional copies when the ICD has been annually reviewed or changed.

A7.1.7. **ICD Legal Letter.** Submit one copy of the endorsed legal letter for each newly approved protocol and ICD, or an ICD that has been administratively changed or revised.

A7.1.8. **OF 310.** Submit one copy of the endorsed OF 310 for each annually reviewed or newly approved protocol. Ensure sections 1-16 of the OF 310 have been completed.

A7.1.9. **IRB Minutes.** Submit one copy of the approved IRB minutes endorsed by the IRB Chairperson and Commander/AIO. Below are sample captions of IRB minutes. It is highly encouraged that this format be used:

A7.1.9.1. New Protocols: **XXX-2000-0001-H, "Title of New Study" (P.I. Lt Col John Smith)** This study has been determined to pose greater than minimal risk to the subject. The research focus area is Treatment Diagnosis, or Other (TDO). Enter pertinent discussion items, such as objectives, funding, or investigational drug/devices. The IRB's recommendations and document the number of votes for or against approval. If Lt Col John Smith is an IRB committee member add ", with Lt Col abstaining." **(CLOSED), (OPEN) (OPR:) (ECD:) or (TABLED) (OPR:) (ECD:)**

A7.1.9.2. Continuing Reviews: **XXX-2000-0001-H, "Title of New Study" (P.I. Lt Col John Smith)** This study has been determined to pose minimal risk to the subject. The research focus area is Medical Utilization. Enter pertinent discussion items, such as PI changes, patient enrollment, and/or funding issues. The committee voted to approve the continuing review of this study with a vote of 5 for and 2 against. **(CLOSED), (OPEN)(OPR:)(ECD:) or (TABLED) (OPR:)(ECD:)**

A7.1.9.3. Changes: **XXX-2000-0001-H, "Title of New Study" (P.I. Lt Col John Smith)** This study has been determined to pose greater than minimal risk to the subject. The research focus area is Prevention. Enter pertinent discussion items, such as protocol or ICD amendments, administrative changes, or revisions. State PI or Medical Monitor changes. The committee decided to table this study until concerns are resolved. **(CLOSED), (OPEN) (OPR:) (ECD:) or (TABLED) (OPR:) (ECD:)**

A7.1.9.4. Closure: **XXX-2000-0001-H, "Title of New Study" (P.I. Lt Col John Smith)**
This study has been determined to pose greater than minimal risk to the subject. The research focus area is Medical Readiness. Enter pertinent discussion items, such as results, publications, or presentations. The committee unanimously voted to close this study. If Lt Col John Smith is an IRB committee member add ", with Lt Col abstaining."
(CLOSED), (OPEN)(OPR:) (ECD:) or (TABLED) (OPR:) (ECD:)

A7.1.9.5. Expedited Reviews: **XXX-2000-0001-H, "Title of New Study" (P.I. Lt Col John Smith)**
This study has been determined to pose no more than minimal risk to the subject and meets the requirements of the common rule for expedited review. The research focus area is Treatment Diagnosis, or Other (TDO). Enter pertinent discussion items. **(CLOSED), (OPEN) (OPR:) (ECD:) or (TABLED) (OPR:) (ECD:)**

A7.1.10. **Commander/AIO Approval.** In most cases, the IRB minutes serve as the document that demonstrates Commander/AIO protocol action approval. In the event the Commander/AIO does not endorse IRB minutes, submit an official memorandum to AFMOA/SGOT with "approval/disapproval" element next to the signature block of the Commander/AIO.

A7.1.11. **Principal Investigator Curriculum Vitae (CV).** For first time investigators, submit one copy of the investigators CV.

Attachment 8**SAMPLE FORMAT FOR PROGRESS/FINAL REPORT**

MEMORANDUM FOR (LOCAL IRB) DATE
AFMOA/SGOT
IN TURN

FROM: Your Facility Name/Address

SUBJECT: Research Protocol (Surgeon General's Assigned Number and Title)

Status of study, including a brief summary of any results (preliminary or final) obtained in the study. If the study is part of a multi-center trial, this should be clarified and any available results provided. Explain any problems or changes with the study i.e. informed consent obtainment/documentation, new information since last review.

When directed by the IRB: Number of male and female subjects accrued to date since activation of the study; number of subjects accrued by ethnic origin and explanation of subject accrual demographics if there appeared to be inequitable recruitment of subjects.

Status of subjects entered into the protocol (benefits/adverse reactions). The number and description of unanticipated adverse event(s) from initial approval of the study to the present (even if these occurred at other multi-center locations). The number of subject withdrawals from the study and the reasons for the withdrawal.

Current risk/benefit assessment of the study. Has anything happened since the last IRB review? Were there any unanticipated risks which may have altered the risk/benefit relationship? Any significant new findings that may relate to the subjects' willingness to continue participation should be provided to the subjects in accordance with 21 CFR 50-25 (b)(5).

Include a copy of the consent form currently in use and submit it with this report ([Attachment 1](#)).

Status of resources allotted for the study. Include comments on funds received from the Surgeon General's Office, if any.

Estimated completion date of the study and percent completed.

For final reports, include the following:

A statement as to whether the objective of the study was met.

A summary of the entire study to include how the findings may benefit the Air Force.

If the study was terminated prior to completion, explain why.

Publications and presentations made ([Attachment 2](#)).

Attachments:

SIGNATURE BLOCK OF INVESTIGATOR

1. ICD
2. Publication/Presentation (for final reports)

Attachment 9**SAMPLE FORMAT FOR MEMORANDUM OF UNDERSTANDING FOR GIFTS OF TECHNICAL ASSISTANCE****MEMORANDUM OF UNDERSTANDING BETWEEN AIR FORCE MEDICAL TREATMENT FACILITY AND DONOR**

Purpose: This Memorandum of Understanding (MOU) is established to coordinate the services of technical assistance provided to the Air Force in support of an Air Force Clinical, Biological, or Behavioral Research study. Technical assistants are defined as employees or agents of nonfederal organizations who provide a wide variety of services to the Air Force in support of a research investigation protocol or program. These services include administrative, technical, or professional support and are provided at no cost to the government.

Reference: AFPD 40-4

Background:**Air Force Information:**

It is Air Force policy to encourage and support clinical, biomedical and behavioral research that contributes to the progress of the biomedical sciences and to the efficiency of the Air Force or other military Medical Services.

The Air Force Surgeon General, or designee, through the Surgeon General's Research Oversight Committee, will review and render an approval or disapproval decision on clinical, biomedical and behavioral research protocols.

Research is an essential component of optimal health care, and consists of organized scientific inquiry into problems involving the health care of Department of Defense beneficiaries. The goals of the Air Force Clinical and Biomedical Research include: Achieving continuous improvement in the quality of subject care. Providing experience in the essential discipline of organized scientific inquiry to personnel whom will ultimately become teaching chiefs and consultants in Air Force MTFs. Strengthening the Graduate Medical Education (GME) program.

Donor Information:

Description of the organization which is making the offer of service(s). (Example: The ABC Organization is a not-for-profit corporation created to encourage and support clinical research and medical education.)

The (donor) is or is not a defense contractor. (Choose one either is or is not.)

The (donor) has the capability to provide the services of trained personnel (professional technical, and administrative) to support Air Force Surgeon General-approved clinical/biological research at (location) at no cost to the government.

Procedures:

Management of clinical investigations technical assistance services: (Donor) may proffer technical assistants in support of the research facility. Such technical assistants must abide by all applicable and Air Force rules and regulations.

(Donor) must ensure that such technical assistants clearly understand that the services rendered will be performed without any form of compensation from the US Government.

(Donor) will provide workman's compensation, pay social security taxes, and provide liability insurance and credentials, when required, on all personnel provided as technical assistants to (AF research facility). The donor agrees to inform the Air Force of any change in its technical assistants insurance coverage during the period of service. The (donor) agrees to indemnify and hold harmless the United States, its agents and employees against all liability resulting from the services of its technical assistants.

NOTE: You should obtain this provision as part of the agreement when possible; however, if you cannot, then decide whether it is in the best interest of the Air Force to enter into the agreement without the hold-harmless clause. You should contact your staff judge advocate or medical law consultant before making this decision.

To avoid the appearance of a conflict of interest Air Force medical personnel assigned to or employed (AF research facility) may only receive financial compensation for participation as a subject of research, provided DoD funds are not used for payment and off duty employment is authorized. (Reference 24 U.S.C. 30)

(Donor) will notify the (AF research facility), in writing, of any proposed offer of technical assistance. Prepare such a letter of proffer for each individual who will provide technical assistance. The letter should include the following: name of individual, the nature of their support, and the expected duration of their participation in the one or more clinical investigation protocols or programs for which support is being proffered.

(Donor) proposals for technical assistance services related to clinical investigation protocols will be approved by the facility Commander.

(Donor) agrees to provide information on the number of technical assistants supporting research efforts at (AF research facility) upon request, as a means of confirming internal Air Force audit information.

Standards of Conduct:

Nothing in this agreement pertaining to clinical investigation, technical assistance, or medical education support obviates Air Force requirements pertaining to prevention of conflict of interest or adherence to standards of conduct.

Agreement:

The Commander (AF research facility), and the (Title of Individual) of (Donor) hereby agree to enter into this MOU to establish procedures for (Donor) to provide technical assistance in support of patient care and research effort at the (AF research facility).

Effective Date:

This agreement becomes effective upon the signature of both parties and remains in effect until canceled.

Modification of This Agreement:

This agreement will be reviewed biennially at least 90 days prior to the anniversary date. It may be revised at any time upon the written mutual consent of the parties concerned.

Termination of Agreement:

This agreement may be terminated at any time by either party concerned, upon giving at least (suggest 90 days) written notice to the other party. Such notice shall be sent by registered mail.

Approval:

Research Facility Commander

Date

Donor (name and title)

Date

Attachment 10

SAMPLE FORMAT LEGAL LETTER

DATE

MEMORANDUM FOR SQUADRON/OFFICE SYMBOL/NAME

FROM: (MEDICAL LEGAL OFFICE SYMBOL)

SUBJECT: Review of Informed Consent Documents

1. Reference the attached Informed Consent Documents for Research Proposals proposed to the Institutional Review Board:

New Protocol Informed Consent Documents:

a. Protocol Number, "Protocol Title."

b. Protocol Number, "Protocol Title."

Revised Protocol Informed Consent Documents:

a. Protocol Number, "Protocol Title."

b. Protocol Number, "Protocol Title."

2. I have reviewed the aforementioned documents IAW AFI 40-402 and found them to be legally sufficient.

SIGNATURE BLOCK

Medical Law Consultant

Attachment 11**SINGLE PROJECT ASSURANCE TEMPLATE****DOD SINGLE PROJECT ASSURANCE**

[Insert Institution Name]

**ASSURANCE OF COMPLIANCE WITH DEPARTMENT OF DEFENSE
REGULATIONS FOR PROTECTION OF HUMAN RESEARCH SUBJECTS**

Using this Template, type on Organizational Letterhead, supplying where indicated, and information specific to the proposed research activity and your organization, including the required certification on the endorsement page.

Assurance of compliance with Department of Defense, Title 32, Code of Federal Regulations, Part 219 (32 CFR 219), "Protection of Human Subjects" and "Protection of Human Subjects in DoD Supported Research," August 19, 1991.

PART 1

[Insert Name of Facility], hereinafter known as the "facility," hereby gives assurance that it will comply with the Department of Defense Regulations for the Protection of Human Subjects (32 CFR 219); Title 10, United States Code, Section 980, Limitation on Use of Humans as Experimental Subjects (hereinafter referred to as 10 USC 980); Air Force Instruction AFI 40-402; DoD Directive DoDD 3216.2; and where applicable, 21 CFR 50, 21 CFR 56, and 45 CFR 46 (Subparts B, C, D) under the authority of the Department of Defense as specified below.

1. Statement of Principles and Policies**a. Ethical Principles**

This facility is guided by the ethical principles regarding all research involving humans as subjects as set forth in the report of the National Commission for the Protection of Human Subjects of Bio medical and Behavioral Research entitled, Ethical Principles and Guidelines for the Protection of Human Subjects of Research (the "Belmont Report"). In addition, the requirements set forth in Title 32 Part 219 of the Code of Federal Regulations (32 CFR 219) will be met for all DoD- supported research.

b. Facility Policy

(1) This facility acknowledges and accepts its responsibilities for protecting the rights and welfare of human subjects of research covered by this assurance.

(2) It is the policy of this facility that, except for research in which the only involvement of human subjects is in one or more of the categories exempted under 32 CFR 219.101(b)(1-6) or 219.101.e of the DoD regulations, this policy is applicable to all research involving human subjects, and all other activities which are even in part such research, if either:

(a) The research is sponsored by this facility, or

(b) The research is conducted by or under the direction of any employee or agent of this facility in connection with his or her facility responsibilities, or

(c) The research is conducted by or under the direction of any employee or agent of this facility using any property or component of this facility, or

(d) The research involves the use of this facility's nonpublic information to identify or contact human research subjects or prospective subjects.

(2) It is the policy of this facility that, except for those categories specifically exempted by 32 CFR 219, no research investigator shall involve any human being as a subject in research unless the research investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. Categories of exemption as defined above {32 CFR 219.101 paragraph (b)(1-6) and paragraph (e)} shall not be confused with minimal risk categories as defined at 32 CFR 219.117. IRB waiver of informed consent, as defined at 32 CFR 219.117, is not permitted within DoD (see Title 10, USC 980). Human subjects research defined as "minimal risk" is permitted expedited review; however, informed consent shall not be waived.

(3) This facility acknowledges and accepts its responsibilities for protecting the rights and welfare of human subjects of research covered by this policy.

(4) This facility assures that before human subjects are involved in research covered by this policy, proper consideration will be given to:

(a) The risks to the subjects,

(b) The anticipated benefits to the subjects and others,

(c) The importance of the knowledge that may reasonably be expected to results, and

(d) The informed consent process to be employed.

(5) This facility acknowledges that it bears full responsibility for the performance of all research involving human subjects, covered by this policy.

(6) This facility bears full responsibility for complying with federal, state, or local laws as they may relate to research covered by this policy.

(7) This facility encourages and promotes constructive communication among the research administrators, department heads, research investigators, clinical care staff, human subjects, and facility officials as a means of maintaining a high level of awareness regarding safeguarding of the rights and welfare of the subjects.

(8) This facility will exercise appropriate administrative overview carried out at least annually to insure that its practices and procedures designed for the protection of the rights and welfare of human subjects are being effectively applied.

(9) This facility will consider additional safeguards in research when that research involves pregnant women, children, other potentially vulnerable groups and human in vitro fertilization.

(10) This facility shall provide each individual at the facility conducting or reviewing human subject research (e.g., research investigators, department heads, research administrators, and research reviewers) with a copy of this statement of ethical principles and policy.

PART 2

Applicability of Assurance and Responsibilities:

In regard to the Protocol/Study/Project entitled, "[Insert Title]", Protocol/Study/Project/Contract Number [Insert Number], submitted on behalf of [Insert Name of Principal Investigator], Principal Investigator, this facility has complied and will continue to comply with the requirements of 32 CFR 219 as specified below.

1. IRB Review

- a. The convened [Insert Name of IRB] IRB reviewed and approved the above Protocol/Study/ Project.
- b. The IRB determined, in accordance with the criteria found at 32 CFR 219.111, and where applicable, 45 CFR 46 Subparts B, C, and D, that protections for human research subjects are adequate.
- c. The IRB has the authority to suspend or terminate approval of research activity in accordance with 32 CFR 219.113 because of (1) noncompliance with 32 CFR 219, this Assurance document, or the IRB's requirements; or (2) unexpected serious harm to subjects.
- d. The IRB has determined that legally effective informed consent (copy of document must be attached) will be obtained in a manner and method which meets the requirements of 32 CFR 219.116 and 219.117, and in the case of research involving children, 32 CFR 219.408.
- e. The IRB shall review, and have the authority to approve, require modification in, or disapprove changes proposed in this research activity.
- f. The IRB shall conduct continuing reviews of all research at intervals appropriate to the degree of risk, but not less than once per year (32 CFR 219.109(e)). The Chairperson at the request of any IRB member or Facility Official to consider any matter concerned with the rights and welfare of any subject may call the IRB into an interim review session.
- g. The IRB shall prepare and maintain adequate documentation of its activities in accordance with 32 CFR 219.115.
- h. The IRB shall report promptly to the facility President [or insert appropriate office here if not President] and AFMSA/SGRC:
 - (1) Any serious or continuing noncompliance by investigators with the requirements of the IRB, and

(2) Any suspension or termination of IRB approval.

i. The IRB shall report promptly to the facility President [or insert appropriate office here if not President] any information received concerning:

(1) Injuries to human subjects,

(2) Unanticipated problems involving risks to subjects or others, and

(3) Any changes in this research activity which are received and approved by the IRB.

2. Research Investigator Reporting Responsibilities

a. Research investigators shall report promptly to the IRB proposed changes in this research activity and the changes shall not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the subjects.

b. Research investigators shall report promptly to the IRB any unanticipated problems involving risks to subjects and others.

3. Facility Responsibilities

a. This facility has provided and will continue to provide both meeting space for the IRB and sufficient staff to support the IRB's review and record keeping duties.

b. This facility shall report promptly to AFMSA/SGRC:

(1) Injuries to human subjects,

(2) Unanticipated problems involving risks to subjects or to other, and

(3) Any changes in this research activity which are reviewed and approved by the IRB and this facility.

c. In addition to the review and approval of the IRB, this facility reviewed and sponsors the project entitled, “[Insert Title].”

d. In accordance with the compositional requirements of section 219.107 of 32 CFR 219, this facility has established an IRB as listed in the attached roster. This IRB is responsible for the initial and continuing review of this activity and will observe the quorum requirements of 32 CFR 219.108.

PART 3

[Insert Facility Name]

Facility certification and endorsement and AFMSA/SGRC approval regarding this Assurance and the Project entitled: “[Insert Title].” Protocol/Study/Project/Contract [Insert Number]

1. I certify that the above Project was reviewed and approved by the [Insert IRB Name] IRB in accordance with the requirements of Part 219, Title 32 of the Code of Federal Regulations and this Assurance of Compliance on (Date of IRB Approval Must Be Inserted).

IRB Chairperson

Signature _____ Date _____

Name and Title: _____

Address: _____

Phone: _____

The Signatory Official must be a senior Facility Official who has the authority to commit the entire facility named in the Assurance application, as well as all of the Facility components to a legally binding agreement. Entities that the Signatory Official is not legally authorized to represent may not be covered under the Assurance. This individual must also have the authority to assure compliance of the Facility and all of its components to the terms of the Assurance. The IRB Chair and IRB members are not appropriate personnel to serve as the Signatory Official.

2. I certify that this facility endorses the above project and abides by the principles, policies, and procedures of Parts 1 and 2 of this Assurance of Compliance.

Authorized Facility Official

Signature _____ Date _____

Name and Title: _____

Address: _____

Phone: _____

Phone: _____

THIS PAGE FOR AFMSA/SGRC USE ONLY

3. All parts of this Assurance are in compliance with the requirements of Part 219, Title 32 of the Code of Federal Regulations; 10 USC 980; AFI 40-402; DoDD 3216.2; and where applicable, 21 CFR 50, 21 CFR 56, and 45 CFR 46 (Subparts B, C, D) under the authority of the Department of Defense

ASSURANCE NUMBER _____

AFMSA/SGRC Approving Official

Signature _____ Date _____

Name: DONNAMARIA ROBINSON, Major, USAF, BSC

Address: HQ AFMSA/SGRC
Office of the Surgeon General
5201 1 Leesburg Pike, Suite 1401
Falls Church, VA 22041
Telephone: (703) 681-7056
FAX: (703) 681-4518

E-Mail Address: Donnamaria.robinson@pentagon.af.mil

This assurance expires **three years** from the date of its approval. It must be updated regularly subject to a change in Signatory Official, the IRB Chair, the IRB membership, or of the policies and procedures to maintain this Single Project Assurance file current. A revised and dated IRB membership roster must be submitted if there is a change in the IRB membership. For its uninterrupted continuation, this Assurance must be renegotiated with AFMSA/SGRC prior to its expiration.

Expiration Date: _____

Attachment 12

**AF/SG POLICY GOVERNING CATEGORIZATION OF RESEARCH,
DEVELOPMENT, TESTING AND EVALUATION (RDT&E) ACTIVITIES AS
“HUMAN RESEARCH”****DEPARTMENT OF THE AIR FORCE****HEADQUARTERS UNITED STATES AIR FORCE****WASHINGTON DC**

April 18, 2005

MEMORANDUM FOR SEE DISTRIBUTION

FROM: HQ USAF/SG 1780 Air Force Pentagon Washington DC 20330-1780

SUBJECT: Interim Policy Governing Categorization of Research, Development, Testing, and Evaluation (RDT&E) Activities as

References: (a) AFI 40-402, Protection of Human Subjects in Biomedical and Behavioral Research

(b) DoDD 3216.2, Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research

(c) 32 CFR 219, Protection of Human Subjects

The Air Force Research, Development, Testing and Evaluation (RDT&E) community has traditionally acted outside the realm of “human research,” regulated by separate requirements, guidelines and oversight (e.g., AFI 91-202, *Safety Investigations and Reports*; AFMAN 91-223, *Aviation Safety Investigations and Reports*; AFI 63-101, *Operations of Capabilities-Based Acquisition System*; DoD Directive 5141.2, *Director of Operational Test and Evaluation [DOT&E]*). Recent guidance from DoD indicates that, though many RDT&E activities are properly classified as non-research, some are considered “human research” requiring AF/SG and human subjects protection oversight. Research is defined as a “systematic investigation, including research, testing, development, and evaluation designed to develop or contribute towards generalizable knowledge.” (Ref. c) While all 2-letters are responsible for ensuring the compliance of activities conducted under their purview, the AF Surgeon General has been delegated the authority to oversee all human research conducted in the AF (both medical and non-medical) and the responsibility to ensure the protection of human subjects. This policy applies to human research funded or conducted by the USAF and provides guidance on categorizing RDT&E activities involving human subjects as either non-research or as human research requiring oversight by the AF/SG and compliance with applicable laws and regulations.

RDT&E activities involving human research could include the biological, behavioral, or psychological study of a human or the effects of a test thereon, such as: test exposure to any agent (e.g., lasers, electromagnetic energy, solvents); deviation from normal daily regimens; and active manipulation of bodily processes, behavior, or the environment in which human factors are measured.

It is surmised that the majority of AF RDT&E activities are non-research. Research and non-research may employ similar investigative methods, but the latter is not intended to test a theory or to produce generalizable knowledge. Examples of activities that are generally either not considered human research or that are exempt from human research regulations (Refs a-c) include:

- a. "Exempt" activities meeting the requirements in 32 CFR 219.101(b), unless otherwise required by the USAF or local policy.
- b. Individual or group training of military personnel such as combat readiness, effectiveness, proficiency, or fitness exercises.
- c. Operational test and evaluation activities where the purpose of the tests is to make assessments regarding the attributes of a weapon, equipment, or munitions, including human/machine interfacing systems related thereto.
- d. Health readiness surveillance, such as activities carried out, under 10 U.S.C. 1074f (medical tracking system for members deployed overseas).
- e. Quality assurance, such as activities covered by 10 U.S.C. 1102 and DoD Directive 6025.13, "Medical Quality Assurance in the Military Health System," May 4, 2004.
- f. Evaluations of the success of established programs in achieving objectives or customer satisfaction surveys, when performed for use by program managers.
- g. Compliance Monitoring: Monitoring for compliance of individuals and organizations with requirements applicable to military, civilian, or contractor personnel or to organizational units. This includes such activities as drug testing, occupational health and safety monitoring, and security clearance reviews.

When considering whether to categorize an activity as non-research, it is crucial to be aware of certain complicating factors. Activities obtaining data on the effects of any non-routine interaction with an individual can be viewed as human research. Non-research activities may include components of research activities that are subject to human subject protection regulations. Publication or presentation of results can indicate intent to make knowledge generalizable, thus characterizing the activity as human research. Complicating factors such as these make it essential that qualified, trained individuals review RDT&E activities in order to determine whether human research is involved.

Each 2-letter shall designate an individual to serve as the organization's Research Reviewer. The designated individual shall be sufficiently qualified through experience, expertise, and training to be able to ascertain the acceptability of the proposed activity, while being sufficiently removed from the activity to avoid the appearance of a conflict of interest. The Research Reviewer shall be responsible for reviewing the 2 letter's activities with humans to determine whether human research is involved and, if so, whether the activity can be classified as "Exempt" from References (a)-(c) as per 32 CFR 219.101. In questionable cases, Research Reviewers shall seek the advice of an AF Institutional Review Board (IRB). All human research activities determined by the Research Reviewer to be non-exempt must be submitted to and approved by an appropriate IRB prior to initiation. Furthermore, the research must be conducted under an assurance of compliance approved by AFMSA/SGRC. The Research Reviewer will maintain reports documenting their determinations. These reports shall summarize all activities reviewed,

state whether they were determined to involve human research, and reference which, if any, Exempt category (32 CFR 219.101) was applied. AFMSA/SGRC will be responsible for review of these reports. The Research Reviewer will be subject to approval, training (See Attachment), and oversight by AFMSA/SGRC who, until a Research Reviewer has been trained, shall perform the Research Reviewer's function. Detailed instructions on reviewing and reporting requirements shall be provided to designated Research Reviewers by AFMSA/SGRC.

AF/SGR, under authority of the AF Surgeon General, may grant exceptions to this policy when deemed appropriate in light of each 2 letter's activities. This policy guidance is not intended to circumvent any applicable code, law, regulation, directive, or instruction, but empowers the responsible organizations via the Research Reviewer process to make independent determinations regarding the applicability of human subjects protection regulations to ensure compliance therewith.

This policy supersedes all previous policy pertaining to this issue. Please direct questions to Col Peter Demitry, Assistant Surgeon General, Modernization, DSN 761-7055.

GEORGE PEACH TAYLOR, JR.

Lieutenant General, USAF, MC, CFS

Surgeon General

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Attachment 13

INTERIM CHANGE (IC) TO AFI 40-402, PROTECTION OF HUMAN SUBJECTS IN RESEARCH**5 MAY 2005****SUMMARY OF REVISIONS**

This instruction supplements 32 CFR 219; 45 CFR 46, Subparts B-D (as adopted by DoDD 3216.2; being under the authority of DoD, the "Secretary of Defense" shall be substituted for the "Secretary of Health and Human Services" throughout); 21 CFR 50, 56, 312, and 812; 10 USC 980; DoDD 3216.2 and DoDD 6000.8. When two or more rules are applicable, the most stringent shall take precedence. This IC changes the name of the publication from *Protection of Human Subjects in Biomedical and Behavioral Research* to *Protection of Human Subjects in Research* (title page); updates OPR office symbol from AFMOA/SGOT to AFMSA/SGRC (throughout); updates the OPR and certified by lines (title page); clarifies that this instruction applies to all human research conducted or supported by the Air Force (paragraph 1.1); details roles and responsibilities of the Surgeon General and includes training requirement (paragraph 2.1); details roles and responsibilities of the Surgeon General's Research Oversight Committee and includes training requirement (paragraph 2.2); details roles and responsibilities of AFMSA/SGRC and includes training requirement (paragraph 2.3); clarifies responsibilities of the commander and his Authorized Institutional Official (AIO), includes training requirement (paragraph 2.5.1); states AIO responsibilities related to review of research misconduct (paragraph 2.5.7); details roles and responsibilities of the Institutional Review Boards, including training requirement and reporting to AFMSA/SGRC (paragraph 2.6); (paragraph 2.7.1.1); includes investigator responsibilities for training (paragraph 2.7.1.1); updates information on Assurances of compliance, including requirements for AFMSA/SGRC approval prior to implementation of change in Assurances and coordination of non-Air Force Assurances through AFMSA/SGRC (paragraph 3.1); details information on the International Single Project Assurance (paragraph 3.1.2.3); clarifies requirement to comply with 45 CFR 46, Subparts B-D, for certain vulnerable populations (paragraph 3.2); clarifies the unequivocal prohibition against using prisoners of war as human subjects (paragraph 3.2.4.1); clarifies that research with biological or chemical warfare agents is generally prohibited (paragraph 3.2.6); updates SGROC procedures for review of protocols (paragraph 3.6.1); updates information on research misconduct as per DoDI 3210.7 (paragraph 3.9.1); and clarifies obligation of contractors for requirements of prior approval of any protocol changes prior to implementation (paragraph 4.1.7).

PROTECTION OF HUMAN SUBJECTS

OPR: AFMSA/SGRC (Maj Donnamaria Robinson)

Certified by: AF/SGR (Col Peter F. Demitry)

Supersedes AFI 40-402, 1 September 2000

1.1. Description. In 1991, the DoD, along with 16 federal agencies, adopted regulations that are known collectively as the Common Federal Rule. Title 32, Code of Federal Regulations, Part 219, "Protection of Human Subjects" applies to all research conducted or supported by the DoD. The Department of Health and Human Services' corollary is Title 45, Code of Federal Regulations, Part 46, Subpart A. These regulations embody the ethical principles of the Belmont Report and the World Medical Association Declaration of Helsinki. This instruction supplements 32 CFR 219 and the Food and Drug Administration's (FDA) complimentary regulations, 21 CFR 50 and 56, and is intended to describe laws, regulations, policies and practices that are unique to research conducted or supported by the U.S. Air Force (USAF). This instruction applies to all human subject research conducted or supported by the Air Force. It applies to research that includes human subjects, whether as the direct object of research or as the indirect object of research in the development and testing of military weapon systems, vehicles, aircraft, and other material. It applies to research activities funded by non-Air Force resources in which the human subjects are Air Force military or civilian personnel. It also applies to Air Force funded studies and non-Air Force funded studies at U.S. military installations.

2.1. The Surgeon General

2.1.1. Is the single point of accountability for the Air Force Human Research Protection Program (HRPP).

2.1.1.1. Completes human subjects protection training established by AFMSA/SGRC.

2.1.1.2. Is responsible for ensuring Air Force compliance with all applicable human subjects protection requirements. Appoints a Surgeon General's Research Oversight Committee (SGROC). Delegates authority to SGROC and AFMSA/SGRC to monitor compliance of the HRPP; this authority cannot be further delegable.

2.1.1.3. Authorizes funds to support the Air Force Clinical, Biomedical, and Behavioral Investigations in accordance with DoDD 6000.8

2.1.1.4. Provides blanket authorization for Air Force medical center participation in the National Cancer Institute's (NCI) Clinical Trials Cooperative Group Program.

2.1.1.5. Shall serve as the final authority on implementation of DoD Instruction 3210.7, Research Integrity and Misconduct. Delegates this function to the lowest possible organizational level that allows an independent, unbiased, and equitable process. Reserves the right to exercise authorities that otherwise would be delegated to local Air Force institutions.

2.1.2. May grant deviations from this instruction consistent with applicable law and supported by adequate justification.

2.2. The Surgeon General's Research Oversight Committee (SGROC)

2.2.1. Ensures compliance with federal policy for the protection of human subjects (32 CFR 219; 45 CFR 46, Subparts B-D; 10 USC 980; DoDD 6000.8; DoDD 3216.2; 21 CFR 50, 56, 312, and 812; and all other applicable requirements related to human subjects protection).

2.2.1.1. Completes human subjects protections training established by AFMSA/SGRC.

2.2.2. Approves, recommends changes, defers or disapproves all research protocols of greater than minimal risk and all amendments to approved protocols adding significant risk, with the

exception of cooperative group oncology studies, for which SGROC either concurs with IRB approval, concurs with changes recommended, or non-concurs. Has the authority to determine exempt status of proposed research activities when deemed necessary and appropriate. Ensures compliance of all other protocols as per paragraph 3.6.1 of this instruction. Reviews serious, unexpected, related adverse event reports and forwards acknowledgement and any necessary recommendations to the IRB in a timely manner.

2.3. The Research and Compliance Office (AFMSA/SGRC)

2.3.1. Is the Air Force administrator for Institutional Assurances of Compliance (Assurances) IAW the Federal Policy for the Protection of Human Subjects. Coordinates, approves and monitors Assurances for all human research conducted or supported by the Air Force. Has the authority to suspend or terminate Assurances in cases of serious non-compliance.

2.3.2. Establishes policies on human subjects protections training to be completed on at least an annual basis by headquarters level personnel, AFMSA/SGRC, SGROC members, and oversight staff to ensure compliance of the Air Force Human Research Protection Program (HRPP). Completes training on at least an annual basis. Ensures that all personnel connected with the human subjects research review process (including but not limited to AFMSA/SGRC staff, the Surgeon General, the Assistant Surgeon General, Modernization, IRB members, IRB administrative staff, investigators, and key research personnel) understand and are qualified to meet their obligation to protect the rights and welfare of human subjects by requiring completion of human subjects protection training prior to involvement with any human research.

2.3.4. Coordinates policy and provides guidance for human research and interprets regulations for the HRPP. Is responsible for keeping the DoD (via DDR&E or designee) informed of significant issues regarding the safety of human subjects, including:

2.3.4.1. Any suspension or termination of a DoD Assurance issued by the Air Force or of any other assurance submitted by the Air Force to another federal entity;

2.3.4.2. Any investigation of the Air Force conducted by an outside entity;

2.3.4.3. Any investigation of a grantee by the Air Force that results in negative findings; and,

2.3.4.4. Significant communication between the Air Force and other federal departments and agencies regarding compliance and oversight.

2.3.5. Monitors funds in support of clinical, biomedical and behavioral research projects as described in section 5.1 below.

2.5.1. Is responsible for ensuring the institutions' compliance with requirements of 32 CFR 219, DODD 3216.2 and this instruction. Alternately, the commander may designate a member of the executive staff to serve as the AIO. The commander or AIO completes on at least an annual basis human subjects protection training established by local policy. The AIO provides a local institutional environment that identifies and strives to reduce the possibility for conflict of interest by personnel responsible for protecting human subjects.

2.5.7. Establishes local written procedures for review of allegations of research misconduct IAW DoDI 3210.7 and this instruction. Reviews any allegations of research misconduct and determines administrative or punitive actions under the Uniform Code of Military Justice. Ensures research activities will be conducted with integrity and according to ethical and legal standards. (Refer to Office of Science and Technology Policy letter published in the Federal Register: October 14, 1999, Volume 64, Number 198, pages 55722-55725). See paragraph 3.9 of this instruction.

2.6.1. Establishes written policies and procedures on human subjects protections training, to be completed by the Institutional Official, IRB members, IRB staff, investigators, and key research personnel on at least an annual basis. Submits training policies to SGROC for approval.

2.6.1.1. Ensures completion of human subjects protection training prior to allowing any person to participate in human subject research or related protection activities.

2.6.10. Reports substantive issues to AFMSA/SGRC, including, but not limited to:

2.6.10.1. Upcoming inspections by the Department of Health and Human Services (DHHS) or FDA when notified and provides inspection results within 30 days of receipt to AFMSA/SGRC;

2.6.10.2. Any suspension or termination of any assurance submitted by the Air Force to another federal entity;

2.6.10.3. Any investigation of the Air Force conducted by an outside entity;

2.6.10.4. Any investigation of a grantee by the Air Force that results in negative findings; and,

2.6.10.5. Significant communication between the Air Force and other federal departments and agencies regarding compliance and oversight.

2.7.1.1 Completes, and requires research personnel to complete, initial and ongoing human subjects protection training established by the IRB.

2.7.7. Submits all proposed changes to IRB for review and approval prior to implementation in accordance with 32 CFR 219.103(b)(4). Substantive changes require prospective review and approval by the AIO. Notifies the IRB of unanticipated problems with ongoing research in a timely manner.

3.1. Assurances. All human research conducted or supported by the Air Force shall be conducted under an Assurance of compliance acceptable to the Air Force, unless the research is exempt from these regulations under 32 CFR 219.101(b). See 32 CFR 219.103(a). A DoD Assurance is required for research performed at DoD facilities and funded by the DoD. A DoD Assurance issued by the Air Force is required for research conducted by the Air Force at an Air Force facility. Any changes to an Assurance covering research conducted or supported by the Air Force must be prospectively approved by AFMSA/SGRC.

3.1.1. DoD Assurances issued by the Air Force. Applications for DoD Assurances issued by the Air Force must be reviewed and approved by AFMSA/SGRC prior to initiation of any human research. Completed applications must be forwarded to AFMSA/SGRC with policies and procedures for local IRB operation, including those governing continuing review of the research. All IRBs designated in DoD Assurances issued by the Air Force must be registered with AFMSA/SGRC along with an IRB membership roster. AFMSA/SGRC shall issue every Assurance a tracking number. The Air Force issues two types of Assurances: the Multiple Project Assurance (MPA) and the Single Project Assurance (SPA).

3.1.1.1 DELETED.

3.1.2. SPA

3.1.2.1. An SPA applies to only one project. Documentation of IRB review and approval of the covered study must be submitted to AFMSA/SGRC along with the SPA application. SPAs are awarded for up to three years, subject to continuing review. A SPA institution that has demonstrated compliance with Assurance requirements may submit application for a MPA.

3.1.2.2. SPA for an Institution Utilizing Another Air Force Institution's IRB. When an institution such as a small clinic does not have an IRB, before conducting human research supported or conducted by the Air Force, it must obtain both a valid DoD Assurance issued by the Air Force and review and approval from a regional Air Force IRB.

3.1.2.3 International Assurance. All research taking place outside of the U.S. and conducted or supported by the Air Force must be conducted under an International Assurance acceptable to AFMSA/SGRC as per paragraph 3.1.4.1. Research conducted at Air Force facilities outside of the U.S. must be conducted under a DoD International SPA issued by the Air Force through AFMSA/AGRC. Due to legal, ethical, and cultural differences between the U.S. and the foreign country in which the research will take place, IRBs, AFMSA/SGRC, and investigators are instructed to take extra care in reviewing, approving, and conducting international research to ensure compliance with the spirit of ethical guidelines for the protection of human research subjects, as well as the letter of the law. See paragraph 3.2.5 of this instruction for additional information on conducting research outside of the U.S.

3.1.3. MPA. An MPA can apply to one or more human research projects.

3.1.3.1. Submit requests for an MPA to AFMSA/SGRC. Requests must include a statement of principles and policies, documentation of IRB review and local policies for IRB operation.

3.1.4. Non-Air Force Assurances. In most cases, a DoD Assurance will be required. However, in some cases, AFMSA/SGRC may accept an Assurance issued by DHHS. Whenever the Air Force accepts an Assurance not issued by the Air Force, the institution must provide a separate written assurance that it will comply with requirements unique to the Air Force, including this instruction and all attachments, and that it will report to the Air Force continuing compliance and safety issues, such as continuing reviews, adverse events, and protocol deviations, in accordance with this instruction.

3.1.4.1. Copies of all non-Air Force Assurances submitted by Air Force institutions must be provided to AFMSA/SGRC in order to ensure proper coordination with the Assurance-granting agency and compliance with the requirements outlined in this instruction.

3.1.4.2. Federalwide Assurance (FWA). DHHS issues FWAs for research funded by DHHS. Institutions participating in NCI Clinical Trials Cooperative Group projects are required to obtain an FWA from DHHS because NCI is an institute within DHHS. Air Force Institutions needing a DHHS FWA should not check the box on the FWA electing to apply the FWA to all of its human research.

3.1.4.3. Cooperative Project Assurance (CPA). A CPA is an Assurance previously issued by DHHS for facilities involved in NCI's Clinical Trials Cooperative Group studies.

3.2. Requirements for Special Categories of Human Subjects. The use of human subjects in research in which there is an intervention or interaction with subjects is limited to persons who are fully informed and who voluntarily agree to participate in the study. If the subject is legally incompetent to give consent (as with infirmed, minors, or patients in an unconscious state) and the proposed measures are intended to benefit the subject, then consent may be obtained from a legal guardian on the subject's behalf. Research supported or conducted by the Department of Defense that affects the following vulnerable populations shall meet the additional protections of 45 CFR 46, Subparts B-D: fetuses, pregnant women, or human in vitro fertilization (Subpart B); prisoners (Subpart C); and minors (Subpart D).

3.2.4.1. Prisoners of War. The use of prisoners of war as research subjects is unequivocally prohibited. See DoD Directive 3216.2, paragraph 4.4.2.

3.2.6. Protocols Involving Biological or Chemical Warfare Agents. Research involving the use of human subjects for testing of chemical or biological warfare agents or nuclear weapons effects is generally prohibited. See DoDD 3216.2, paragraph 4.4.5., and 50 USC 1520a. Such research must be submitted to OUSDAT for approval prior to implementation.

3.6.1. The SGROC must review and approve all greater than minimal risk protocols prior to initiation except as noted in [3.6.2](#) below. Protocols that are determined by the IRB to be no more than minimal risk to the subject must be sent to AFMSA/SGRC, which shall conduct audits in order to ensure compliance. Minimal risk studies may begin upon local IRB and Commander/AIO approval. Protocols that are determined to be exempt by the IRB Chair or designee must be evaluated using written criteria, reported to AFMSA/SGRC, and documented in the IRB minutes and in section 8 of the OF 310. The exemption must be referenced using the appropriate CFR rule. The OF 310 must be kept on file for audit purposes. If the SGROC disagrees with the IRB's determination, the research study may be temporarily suspended until resolution. Guidance for document submission to the SGROC is included in this instruction ([Attachment 7](#)).

3.9.1. Air Force institutions must ensure that research is conducted under the highest ethical standards. In support of this responsibility, every allegation of research misconduct shall be investigated. All allegations of research misconduct shall be investigated in an independent, unbiased, and equitable manner that minimizes disruption to research in process unless the research misconduct could result in a threat to public health or safety. Written institutional policy governing research misconduct must be established in accordance with the requirements of DoDI 3210.7 and submitted to AFMSA/SGRC.

3.9.1.3. All allegations of research misconduct occurring within an institution shall be referred to and investigated by the AIO; however, SGR may investigate the allegation if there is a determination that 1) the institution is unable to conduct a thorough and unbiased inquiry and/or

investigation; 2) it is in the public interest for the parent command to conduct the inquiry and investigation; or 3) the allegation involves a small institution or an individual that cannot reasonably be expected to respond. SGR shall investigate allegations of research misconduct occurring outside of an Air Force institution.

4.1.7. Contractors must notify the US Air Force contracting agency and obtain IRB approval of any changes to the protocol prior to implementation. Contractors must have written procedures for notifying the US Air Force contracting agency of any misadventure or unanticipated adverse medical event that coincides with or possibly results from using human subjects in a US Air Force-sponsored research protocol. Include all the information required in paragraph 2.7 of this instruction.

Attachment 11

SINGLE PROJECT ASSURANCE TEMPLATE

DOD SINGLE PROJECT ASSURANCE

[Insert Institution Name]

ASSURANCE OF COMPLIANCE WITH DEPARTMENT OF DEFENSE REGULATIONS FOR PROTECTION OF HUMAN RESEARCH SUBJECTS

Using this Template, type on Organizational Letterhead, supplying where indicated, and information specific to the proposed research activity and your organization, including the required certification on the endorsement page.

Assurance of compliance with Department of Defense, Title 32, Code of Federal Regulations, Part 219 (32 CFR 219), "Protection of Human Subjects" and "Protection of Human Subjects in DoD Supported Research," August 19, 1991.

PART 1

[Insert Name of Facility], hereinafter known as the "facility," hereby gives assurance that it will comply with the Department of Defense Regulations for the Protection of Human Subjects (32 CFR 219); Title 10, United States Code, Section 980, Limitation on Use of Humans as Experimental Subjects (hereinafter referred to as 10 USC 980); Air Force Instruction AFI 40-402; DoD Directive DoDD 3216.2; and where applicable, 21 CFR 50, 21 CFR 56, and 45 CFR 46 (Subparts B, C, D) under the authority of the Department of Defense as specified below.

1. Statement of Principles and Policies

a. Ethical Principles

This facility is guided by the ethical principles regarding all research involving humans as subjects as set forth in the report of the National Commission for the Protection of Human Subjects of Bio medical and Behavioral Research entitled, Ethical Principles and Guidelines for the Protection of Human Subjects of Research (the "Belmont Report"). In addition, the requirements set forth in Title 32 Part 219 of the Code of Federal Regulations (32 CFR 219) will be met for all DoD- supported research.

b. Facility Policy

(1) This facility acknowledges and accepts its responsibilities for protecting the rights and welfare of human subjects of research covered by this assurance.

(2) It is the policy of this facility that, except for research in which the only involvement of human subjects is in one or more of the categories exempted under 32 CFR 219.101(b)(1-6) or 219.101.e of the DoD regulations, this policy is applicable to all research involving human subjects, and all other activities which are even in part such research, if either:

(a) The research is sponsored by this facility, or

(b) The research is conducted by or under the direction of any employee or agent of this facility in connection with his or her facility responsibilities, or

(c) The research is conducted by or under the direction of any employee or agent of this facility using any property or component of this facility, or

(d) The research involves the use of this facility's nonpublic information to identify or contact human research subjects or prospective subjects.

(2) It is the policy of this facility that, except for those categories specifically exempted by 32 CFR 219, no research investigator shall involve any human being as a subject in research unless the research investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. Categories of exemption as defined above {32 CFR 219.101 paragraph (b)(1-6) and paragraph (e)} shall not be confused with minimal risk categories as defined at 32 CFR 219.117. IRB waiver of informed consent, as defined at 32 CFR 219.117, is not permitted within DoD (see Title 10, USC 980). Human subjects research defined as "minimal risk" is permitted expedited review; however, informed consent shall not be waived.

(3) This facility acknowledges and accepts its responsibilities for protecting the rights and welfare of human subjects of research covered by this policy.

(4) This facility assures that before human subjects are involved in research covered by this policy, proper consideration will be given to:

(a) The risks to the subjects,

(b) The anticipated benefits to the subjects and others,

(c) The importance of the knowledge that may reasonably be expected to results, and

(d) The informed consent process to be employed.

(5) This facility acknowledges that it bears full responsibility for the performance of all research involving human subjects, covered by this policy.

(6) This facility bears full responsibility for complying with federal, state, or local laws as they may relate to research covered by this policy.

(7) This facility encourages and promotes constructive communication among the research administrators, department heads, research investigators, clinical care staff, human subjects, and facility officials as a means of maintaining a high level of awareness regarding safeguarding of the rights and welfare of the subjects.

(8) This facility will exercise appropriate administrative overview carried out at least annually to insure that its practices and procedures designed for the protection of the rights and welfare of human subjects are being effectively applied.

(9) This facility will consider additional safeguards in research when that research involves pregnant women, children, other potentially vulnerable groups and human in vitro fertilization.

(10) This facility shall provide each individual at the facility conducting or reviewing human subject research (e.g., research investigators, department heads, research administrators, and research reviewers) with a copy of this statement of ethical principles and policy.

PART 2

Applicability of Assurance and Responsibilities:

In regard to the Protocol/Study/Project entitled, “[Insert Title]”, Protocol/Study/Project/Contract Number [Insert Number], submitted on behalf of [Insert Name of Principal Investigator], Principal Investigator, this facility has complied and will continue to comply with the requirements of 32 CFR 219 as specified below.

1. IRB Review

- a. The convened [Insert Name of IRB] IRB reviewed and approved the above Protocol/Study/Project.
- b. The IRB determined, in accordance with the criteria found at 32 CFR 219.111, and where applicable, 45 CFR 46 Subparts B, C, and D, that protections for human research subjects are adequate.
- c. The IRB has the authority to suspend or terminate approval of research activity in accordance with 32 CFR 219.113 because of (1) noncompliance with 32 CFR 219, this Assurance document, or the IRB’s requirements; or (2) unexpected serious harm to subjects.
- d. The IRB has determined that legally effective informed consent (copy of document must be attached) will be obtained in a manner and method which meets the requirements of 32 CFR 219.116 and 219.117, and in the case of research involving children, 32 CFR 219.408.
- e. The IRB shall review, and have the authority to approve, require modification in, or disapprove changes proposed in this research activity.

f. The IRB shall conduct continuing reviews of all research at intervals appropriate to the degree of risk, but not less than once per year (32 CFR 219.109(e)). The Chairperson at the request of any IRB member or Facility Official to consider any matter concerned with the rights and welfare of any subject may call the IRB into an interim review session.

g. The IRB shall prepare and maintain adequate documentation of its activities in accordance with 32 CFR 219.115.

h. The IRB shall report promptly to the facility President [or insert appropriate office here if not President] and AFMSA/SGRC:

(1) Any serious or continuing noncompliance by investigators with the requirements of the IRB, and

(2) Any suspension or termination of IRB approval.

i. The IRB shall report promptly to the facility President [or insert appropriate office here if not President] any information received concerning:

(1) Injuries to human subjects,

(2) Unanticipated problems involving risks to subjects or others, and

(3) Any changes in this research activity which are received and approved by the IRB.

2. Research Investigator Reporting Responsibilities

a. Research investigators shall report promptly to the IRB proposed changes in this research activity and the changes shall not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the subjects.

b. Research investigators shall report promptly to the IRB any unanticipated problems involving risks to subjects and others.

3. Facility Responsibilities

a. This facility has provided and will continue to provide both meeting space for the IRB and sufficient staff to support the IRB's review and record keeping duties.

b. This facility shall report promptly to AFMSA/SGRC:

(1) Injuries to human subjects,

(2) Unanticipated problems involving risks to subjects or to other, and

(3) Any changes in this research activity which are reviewed and approved by the IRB and this facility.

c. In addition to the review and approval of the IRB, this facility reviewed and sponsors the project entitled, "[Insert Title]."

d. In accordance with the compositional requirements of section 219.107 of 32 CFR 219, this facility has established an IRB as listed in the attached roster. This IRB is responsible for the initial and continuing review of this activity and will observe the quorum requirements of 32 CFR 219.108.

PART 3

[Insert Facility Name]

Facility certification and endorsement and AFMSA/SGRC approval regarding this Assurance and the Project entitled: “[Insert Title].” Protocol/Study/Project/Contract [Insert Number]

1. I certify that the above Project was reviewed and approved by the [Insert IRB Name] IRB in accordance with the requirements of Part 219, Title 32 of the Code of Federal Regulations and this Assurance of Compliance on (Date of IRB Approval Must Be Inserted).

IRB Chairperson

Signature _____ Date _____

Name and Title: _____

Address: _____

Phone: _____

The Signatory Official must be a senior Facility Official who has the authority to commit the entire facility named in the Assurance application, as well as all of the Facility components to a legally binding agreement. Entities that the Signatory Official is not legally authorized to represent may not be covered under the Assurance. This individual must also have the authority to assure compliance of the Facility and all of its components to the terms of the Assurance. The IRB Chair and IRB members are not appropriate personnel to serve as the Signatory Official.

2. I certify that this facility endorses the above project and abides by the principles, policies, and procedures of Parts 1 and 2 of this Assurance of Compliance.

Authorized Facility Official

Signature _____ Date _____

Name and Title: _____

Address: _____

Phone: _____

Phone: _____

THIS PAGE FOR AFMSA/SGRC USE ONLY

3. All parts of this Assurance are in compliance with the requirements of Part 219, Title 32 of the Code of Federal Regulations; 10 USC 980; AFI 40-402; DoDD 3216.2; and where applicable, 21 CFR 50, 21 CFR 56, and 45 CFR 46 (Subparts B, C, D) under the authority of the Department of Defense

ASSURANCE NUMBER _____

AFMSA/SGRC Approving Official

Signature_____Date_____

Name: DONNAMARIA ROBINSON, Major, USAF, BSC

Address: HQ AFMSA/SGRC
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This assurance expires **three years** from the date of its approval. It must be updated regularly subject to a change in Signatory Official, the IRB Chair, the IRB membership, or of the policies and procedures to maintain this Single Project Assurance file current. A revised and dated IRB membership roster must be submitted if there is a change in the IRB membership. For its uninterrupted continuation, this Assurance must be renegotiated with AFMSA/SGRC prior to its expiration.

Expiration Date:_____

ATTACHMENT 12

AF/SG Policy Governing Categorization of Research, Development, Testing and Evaluation (RDT&E) Activities as “Human Research”

DEPARTMENT OF THE AIR FORCE

HEADQUARTERS UNITED STATES AIR FORCE

WASHINGTON DC

April 18, 2005

MEMORANDUM FOR SEE DISTRIBUTION

FROM: HQ USAF/SG 1780 Air Force Pentagon Washington DC 20330-1780

SUBJECT: Interim Policy Governing Categorization of Research, Development, Testing, and Evaluation (RDT&E) Activities as

- References:
- (a) AFI 40-402, Protection of Human Subjects in Biomedical and Behavioral Research
 - (b) DoDD 3216.2, Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research
 - (c) 32 CFR 219, Protection of Human Subjects

The Air Force Research, Development, Testing and Evaluation (RDT&E) community has traditionally acted outside the realm of “human research,” regulated by separate requirements, guidelines and oversight (e.g., AFI 91-202, *Safety Investigations and Reports*; AFMAN 91-223, *Aviation Safety Investigations and Reports*; AFI 63-101, *Operations of Capabilities-Based*

Acquisition System; DoD Directive 5141.2, *Director of Operational Test and Evaluation [DOT&E]*). Recent guidance from DoD indicates that, though many RDT&E activities are properly classified as non-research, some are considered “human research” requiring AF/SG and human subjects protection oversight. Research is defined as a “systematic investigation, including research, testing, development, and evaluation designed to develop or contribute towards generalizable knowledge.” (Ref. c) While all 2-letters are responsible for ensuring the compliance of activities conducted under their purview, the AF Surgeon General has been delegated the authority to oversee all human research conducted in the AF (both medical and non-medical) and the responsibility to ensure the protection of human subjects. This policy applies to human research funded or conducted by the USAF and provides guidance on categorizing RDT&E activities involving human subjects as either non-research or as human research requiring oversight by the AF/SG and compliance with applicable laws and regulations.

RDT&E activities involving human research could include the biological, behavioral, or psychological study of a human or the effects of a test thereon, such as: test exposure to any agent (e.g., lasers, electromagnetic energy, solvents); deviation from normal daily regimens; and active manipulation of bodily processes, behavior, or the environment in which human factors are measured.

It is surmised that the majority of AF RDT&E activities are non-research. Research and non-research may employ similar investigative methods, but the latter is not intended to test a theory or to produce generalizable knowledge. Examples of activities that are generally either not considered human research or that are exempt from human research regulations (Refs a-c) include:

- a. “Exempt” activities meeting the requirements in 32 CFR 219.101(b), unless otherwise required by the USAF or local policy.
- b. Individual or group training of military personnel such as combat readiness, effectiveness, proficiency, or fitness exercises.
- c. Operational test and evaluation activities where the purpose of the tests is to make assessments regarding the attributes of a weapon, equipment, or munitions, including human/machine interfacing systems related thereto.
- d. Health readiness surveillance, such as activities carried out, under 10 U.S.C. 1074f (medical tracking system for members deployed overseas).
- e. Quality assurance, such as activities covered by 10 U.S.C. 1102 and DoD Directive 6025.13, "Medical Quality Assurance in the Military Health System," May 4, 2004.
- f. Evaluations of the success of established programs in achieving objectives or customer satisfaction surveys, when performed for use by program managers.
- g. Compliance Monitoring: Monitoring for compliance of individuals and organizations with requirements applicable to military, civilian, or contractor personnel or to organizational units. This includes such activities as drug testing, occupational health and safety monitoring, and security clearance reviews.

When considering whether to categorize an activity as non-research, it is crucial to be aware of certain complicating factors. Activities obtaining data on the effects of any non-routine interaction with an individual can be viewed as human research. Non-research activities may include components of research activities that are subject to human subject protection regulations. Publication or presentation of results can indicate intent to make knowledge generalizable, thus characterizing the activity as human research. Complicating factors such as these make it essential that qualified, trained individuals review RDT&E activities in order to determine whether human research is involved.

Each 2-letter shall designate an individual to serve as the organization's Research Reviewer. The designated individual shall be sufficiently qualified through experience, expertise, and training to be able to ascertain the acceptability of the proposed activity, while being sufficiently removed from the activity to avoid the appearance of a conflict of interest. The Research Reviewer shall be responsible for reviewing the 2 letter's activities with humans to determine whether human research is involved and, if so, whether the activity can be classified as "Exempt" from References (a)-(c) as per 32 CFR 219.101. In questionable cases, Research Reviewers shall seek the advice of an AF Institutional Review Board (IRB). All human research activities determined by the Research Reviewer to be non-exempt must be submitted to and approved by an appropriate IRB prior to initiation. Furthermore, the research must be conducted under an assurance of compliance approved by AFMSA/SGRC. The Research Reviewer will maintain reports documenting their determinations. These reports shall summarize all activities reviewed, state whether they were determined to involve human research, and reference which, if any, Exempt category (32 CFR 219.101) was applied. AFMSA/SGRC will be responsible for review of these reports. The Research Reviewer will be subject to approval, training (See Attachment), and oversight by AFMSA/SGRC who, until a Research Reviewer has been trained, shall perform the Research Reviewer's function. Detailed instructions on reviewing and reporting requirements shall be provided to designated Research Reviewers by AFMSA/SGRC.

AF/SGR, under authority of the AF Surgeon General, may grant exceptions to this policy when deemed appropriate in light of each 2 letter's activities. This policy guidance is not intended to circumvent any applicable code, law, regulation, directive, or instruction, but empowers the responsible organizations via the Research Reviewer process to make independent determinations regarding the applicability of human subjects protection regulations to ensure compliance therewith.

This policy supersedes all previous policy pertaining to this issue. Please direct questions to Col Peter Demitry, Assistant Surgeon General, Modernization, DSN 761-7055.

GEORGE PEACH TAYLOR, JR.

Lieutenant General, USAF, MC, CFS

Surgeon General

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