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59TH MEDICAL WING

59TH MEDICAL WING INSTRUCTION
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Health Services

HUMAN RESEARCH PROTECTION PROGRAM

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This instruction implements Air Force Policy Directive 41-1, *Health Care Programs and Resources.* The 59th Medical Wing (MDW) has established policies and procedures to delineate the regulatory authority, purpose, principles, functions, and operations of the 59 MDW Human Research Protection Program (HRPP) and the 59 MDW Institutional Review Board (IRB), a component of the 59 MDW HRPP, for protecting the rights and welfare of human subjects in 59 MDW supported and conducted research. This instruction applies to all services and components assigned, attached, or under contract to the 59 MDW. This instruction is not applicable to 59 MDW personnel covered under the Department of Defense (DoD) Assurance for the Protection of Human Research Subjects ("DoD Assurance") and HRPP of another DoD institution while conducting non-exempt research involving human subjects. Refer recommended changes and questions about this publication to the Office of Primary Responsibility using 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 (IAW) Air Force Manual 33-363 *Management of Records* and disposed of IAW Air Force Records Information Management System Records Disposition Schedule.

1. Overview.

1.1. Research is a foundational component of the 59 MDW mission that spans across all 59 MDW institutional health care, medical education, and operational readiness platforms. The 59 MDW has established an institution-wide human research protection program that is both dynamic and unified to ensure all human research activities are regulatory-compliant and

conducted under the highest ethical standards and integrity for the protection and safety of human research subjects.

1.2. The ethical conduct of research is a shared responsibility requiring cooperation, collaboration, and effective communication. A seamless, interwoven relationship within the HRPP, to include organizational officials, HRPP Steering Committee members, investigators, and the 59 MDW IRB, is essential for creating an institutional culture of mutual respect and trust for a unified HRPP across the 59 MDW.

2. Ethical Principles for Conducting Human Research.

2.1. The 59 MDW Institutional Official (IO), Authorized Institutional Official (AIO), IRB, Office of Research Protocol Support, investigators, research staff, and other institutional personnel supporting research will ensure that all of their research-associated activities involving human subjects are guided by the ethical principles set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research entitled, *Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, also known as "The Belmont Report".

2.2. The 59 MDW acknowledges its institutional responsibilities for protecting the rights and welfare of human research subjects. The 59 MDW recognizes the ethical principles of respect for persons, beneficence, and justice, as stated in *The Belmont Report*, and will act in accordance with these principles in all human research to satisfy these responsibilities and to demonstrate HRPP accountability:

2.2.1. Respect for Persons. Individuals should be treated as autonomous agents, and persons with diminished autonomy are entitled to protection.

2.2.2. Beneficence. (1) Do no harm and (2) maximize possible benefits and minimize possible harms.

2.2.3. Justice. The equitable selection of subjects and the equal treatment of all subjects and populations.

3. Institutional Compliance with Laws, Regulations, Policies, and Guidelines.

3.1. The 59 MDW shall enact policies, and procedures (e.g., regulations, instructions, guidelines, and standard operating procedures) necessary to ensure that research involving human subjects is conducted ethically and in accordance with applicable federal, DoD, Air Force (AF), state, and local laws, regulations, and policies (Attachment 1). These regulatory documents will be made available for those involved in conducting or supporting research involving human subjects at the 59 MDW, including other DoD or non-DoD collaborating sites for which the 59 MDW IRB is the IRB of Record.

3.2. The 59 MDW has a DoD Assurance for the Protection of Human Research Subjects (F50007) which authorizes the institution to become engaged in DoD-supported or DoD-conducted non-exempt human research. Additionally, the 59 MDW has a Federal Wide Assurance (FWA) for the Protection of Human Subjects (FWA #00001750) with the Office of Human Research Protections (OHRP) which authorizes the institution to become engaged in Department of Health and Human Services (DHHS)-supported or conducted non-exempt human research.

3.3. Except when research is exempt or not subject to the requirements of the Common Rule, the 59 MDW DoD Assurance applies to all research involving human subjects.

3.4. When the 59 MDW becomes engaged in DHHS-funded research to which its FWA applies, the 59 MDW HRPP and its IRB component will comply with the Common Rule and with additional research protections required for vulnerable populations, as stated in Title 45, Code of Federal Regulations, Part 46, *Public Welfare, Protection of Human Subjects*, Subparts B-D and in Title 10 United States Code Section 980, *Limitation on Use of Humans as Experimental Subjects*.

3.5. When the 59 MDW becomes engaged in research subject to the Food and Drug Administration (FDA) regulations, the 59 MDW HRPP and its IRB component will comply with the Common Rule and with additional research protections required under 10 USC § 980; Title 21 Code of Federal Regulations, Part 50, *Protection of Human Subjects;* Title 21 Code of Federal Regulations, Part 56, *Institutional Review Board*; Title 21 Code of Federal Regulations, Part 312, *Investigational New Drug Application*; Title 21 Code of Federal Regulations, Part 600, *Biological Products*; Title 21 Code of Federal Regulations, Part 812, *Investigational Device Exemptions;* Title 32 Code of Federal Regulations, Part 219, *Protection of Human Subjects.*

3.6. When the 59 MDW becomes engaged in research supported by another DoD Component (e.g., Army, Navy, Coast Guard, and Marines), the 59 MDW and its IRB may be required to comply with policies and procedures of the other DoD Component.

3.7. When the 59 MDW collaborates with other non-DoD investigators who are not employed by an institution with an assurance (non-assured institution), the 59 MDW may extend the applicability of its DoD Assurance to the collaborating investigators through the use of a DoD Individual Investigator Agreement.

3.8. When the 59 MDW relies upon another institution's IRB, or when another institution relies upon the 59 MDW IRB, there must be a written agreement defining the responsibilities and authorities of each organization in complying with the terms of each institution's FWA or DoD Assurance and with 10 USC § 980, DoDI 3216.02, *Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research*, and DoDI 3216.02_AFI 40-402, *Protection of Human Subjects and Adherence to Ethical Standards in Air Force Supported Research*. The existence of a DoD Institutional Agreement for IRB Review (IAIR) satisfies the federal and DoD assurance requirements, as stated in 32 CFR 219 Part 103(b) (2-5).

4. Institutional Roles, Responsibilities, and Authority.

4.1. Active institutional support, mutual trust, cooperation, and dedication by all 59 MDW staff members are the essential foundational elements for a successful and ethical 59 MDW HRPP. It is the responsibility of all individuals covered under the 59 MDW HRPP to understand and apply their obligation to protect the rights and welfare of human research subjects.

4.2. Institutional Official (IO). DoDI 3216.02_AFI 40-402 designates the most senior official, the 59 MDW Commander, as the HRPP IO under the authority, direction, and control of the Head of the Office of the Secretary of Defense and Head of the Office of the Secretary of the Air Force. The IO is responsible for the duties listed in DoDI 3216.02_AFI

40-402 Enclosure 2, §6, including establishing, updating, maintaining, and obtaining approval for the DoD Assurance and any other appropriate Federal assurance. They are also responsible for the additional duties below:

4.2.1. Complete the "Office of the Assistant Secretary of Defense (OASD) Research and Engineering (R&E) Minimum Education Requirements for DoD Personnel Involved in Human Research Protection" Institutional Official training through Air Force Medical Support Agency (AFMSA)/SGE-C in accordance with DoDI 3216.02_AFI 40-401, Enclosure 2, §5.k.

4.2.2. Legally authorized to represent the institution on all matters associated with research involving human subjects in accordance with federal, state, and local laws, and DoD and USAF regulations.

4.2.3. Ensures that the 59 MDW IRB functions independently as an autonomous committee and the IRB Chair, co-Chairs, and IRB members have direct access to the IO and AIO to report if they experience intimidation, undue influence, or coercion in administering their IRB duties or if they have concerns about the function of the 59 MDW HRPP.

4.2.4. Provides an IO "open door" policy for 59 MDW staff, investigators, and other research institutions to identify suspensions or terminations of research, possible unanticipated problems involving risk, serious or continuing research noncompliance, research misconduct, regulatory complaints, acts of coercion or undue influence, etc.

4.3. 59 MDW AIO. The 59 MDW point of contact for all daily operations of the institution's HRPP, to include open communication with OHRP, FDA, and other DoD and federal agencies, as applicable, to address any issue(s) pertaining to the protection of human research subjects. The AIO is responsible for the duties listed in DoDI 3216.02_AFI 40-402 Enclosure 2, § 6, with the exception of establishing, updating, maintaining, and obtaining approval for the DoD Assurance or any other Federal Assurance. They are also responsible for the additional duties below:

4.3.1. Complete "OASD (R&E) Minimum Education Requirements for DoD Personnel Involved in Human Research Protection" Institutional Official training through AFMSA/SGE-C in accordance with DoDI 3216.02_AFI 40-401, Enclosure 2, §5.k.

4.3.2. Ensures effective institution-wide communication and guidance for investigators and staff on research involving human subjects. Ensures that open channels of communication are maintained between components of the HRPP.

4.3.3. Makes recommendations to the IO regarding adequate personnel, space, and other resources needed to support the institution's HRPP.

4.3.4. Point of contact to review and sign regulatory documents for the institution's HRPP, to include reports to OHRP, FDA, DoD Components and other federal agencies, as applicable, also AIO Authorization Letters, agreements to establish reliance on IRBs of Record for collaborative research (e.g., IAIRs), agreements to extend the 59 MDW DoD Assurance coverage to unaffiliated individual investigators (e.g., Individual Investigator Agreements), IRB Minutes, etc.

4.3.5. Primary OPR for routing the following Medical Wing Instructions (MDWIs) for publication approval: 59 MDWI 40-401, *Research Misconduct*, this Instruction, and Operating Instructions (OIs) for the IRB and HRPP.

4.3.6. Ensures implementation of the HRPP throughout the institution and ensures all activities associated with research involving human subjects (as defined by 32 CFR 219 and DoDI 3216.02_AFI 40-402) are guided by respect, conscience, and the ethical principles set forth in *The Belmont Report*.

4.3.7. Ensures the IRB Chair, co-Chairs, and IRB members have direct access to the IO and AIO to report if they experience intimidation, undue influence, or coercion in administering their IRB duties or if they have concerns about the function of the 59 MDW IRB.

4.3.8. Provides an AIO "open door" policy for 59 MDW staff, investigators, and other research institutions to identify suspensions or terminations of research, possible unanticipated problems involving risk, serious or continuing research noncompliance, research misconduct, regulatory complaints, acts of coercion or undue influence, etc.

4.3.9. Appoints the IRB Chair, co-Chairs, and IRB members to the institution's IRB. Assists, where feasible, in identifying qualified subject matter experts, non-scientific, and unaffiliated personnel to help support IRB review and oversight functions.

4.3.10. Oversees the periodic performance evaluation of the IRB Chair, co-Chairs, IRB members, and administrative staff engaged in the oversight of research involving human subjects.

4.3.11. Suspends or terminates the IRB membership for any individual not fulfilling membership responsibilities and/or obligations.

4.3.12. As directed through this Instruction, the AIO approves HRPP Operating Instructions development to further define local policy for implementation of human research protection throughout the organization.

4.4. 59 MDW Institutional Review Board. A component of the HRPP, the 59 MDW IRB is an independent board that will provide initial and continuing review for all research/clinical investigations involving human subjects except for those protocols that meet the criteria for exemption from prior IRB review, based on 32 CFR 219.101(b) (1-6) and 21 CFR 56.104, conducted by the 59 MDW or other DoD or non-DoD institutions, regardless of location or funding source, for which it is the IRB of Record. The IO/AIO may impose additional restrictions to an IRB determination, but cannot approve research that the IRB has not approved and cannot reduce the restrictions imposed by the IRB. The IRB also acts as the 59 MDW Research Privacy Board responsible for reviewing and approving Health Insurance Portability and Accountability Act (HIPAA) Authorizations and HIPAA Waiver requests for research involving human subjects. Decisions are made on the following, but are not limited to: initial study reviews; amendments; progress reports; reports of Unanticipated Problems Involving Risk to Subjects or Others (UPIRSOs); protocol deviations; and substantive complaints from study participants. IRB responsibilities and duties are carried out IAW federal, DoD, AF, state, and local regulations and policies (see Attachment 1).

4.4.1. Non-exempt human research may not start without approval from an IRB designated by the 59 MDW. The IRB has the authority to:

4.4.1.1. Review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by 32 CFR Part 219.

4.4.1.2. Require that information given to subjects as part of informed consent is in accordance with 32 CFR Part 219 § 116. The IRB may require that information, in addition to that specifically mentioned in 32 CFR Part 219 § 116, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects.

4.4.1.3. Require documentation of informed consent or may waive documentation based on 32 CFR Part 219 § 116, with the exception as stated in 10 USC § 980.

4.4.1.4. Notify investigators and the institution in writing of its decision to approve or disapprove a proposed research activity or of modifications required to secure IRB approval of a research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

4.4.1.5. Conduct continuing review of research covered by CFR Part 219 at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.

4.4.1.6. Conduct expedited review of research in accordance with 32 CFR Part 219 § 116.

4.4.1.7. Suspend and/or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head.

4.4.1.8. Make determinations on whether activities are not research, are exempt research, or are research requiring IRB approval in accordance with DoDI 3216.02_AFI 40-402, Enclosure 3, §3.a.(1).(a).

4.4.2. All decisions of the 59 MDW IRB, in accordance with this HRPP policy, as well as, its own policies and procedures, shall be accepted as binding conditions in order to proceed with research involving human subjects. An official or institutional entity cannot approve research that has been disapproved by the IRB (e.g., an IRB disapproval of a protocol cannot be overturned).

4.4.3. The research that has been approved by the IRB must also be approved by the IO/AIO for the institution. The IO/AIO may approve, disapprove, or require additional safeguards to secure approval, or refer the protocol to AFMSA/SGE-C for a regulatory compliance determination. The IO/AIO may not reduce the IRB-approved safeguards or conditions and may not approve research that has not been approved by the IRB. In addition to IO/AIO approval, greater-than-minimal risk research must be approved by AFMSA/SGE-C prior to implementation of the study.

4.4.4. The 59 MDW IRB also has the additional authority to:

4.4.4.1. Make determinations on allegations of non-compliance, including serious and continuing non-compliance, with 59 MDW research policies or federal, DoD, or AF research regulations for the protection of human subjects. Where corrective action is needed, the IRB may take appropriate actions such as, requiring study or informed consent modifications, determining data collected cannot be used for publication, suspending or terminating IRB approval, requiring additional investigator education, disqualifying investigators from conducting research involving human subjects at the institution, and/or recommending to the institution's IO/AIO that further administrative action be taken. The IRB's action shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head. The IRB will not make determinations of research misconduct.

4.4.4.2. Make determinations on allegations or reports of Adverse Events, Serious Adverse Events, Unanticipated Adverse Device Effects, and UPIRSOs. Where corrective action is needed, the IRB may take appropriate actions such as, requiring study or informed consent modifications, determining data collected cannot be used for publication, suspending or terminating IRB approval, requiring additional investigator education, disqualifying investigators from conducting human research at the institution, and/or recommending to the IO/AIO that further administrative action be taken. Any such determination shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, the department or agency head, and other federal agencies, as required. Certain findings are reported to AFMSA/SGE-C to ensure documentation of oversight of IRB determinations. The IRB will not make determinations of research misconduct.

4.4.4.3. Conduct scientific and technical reviews, including reviews of Investigational New Drug (IND) use, Investigational Device Exemptions (IDE), Exempt IDE use, Abbreviated IDE use, and Off-Label use of FDA-approved drugs and devices.

4.4.4.4. Conduct: ethics reviews; HIPAA privacy and confidentiality of data reviews; legal reviews; Data Use Agreement reviews; De-Identified Data Use Agreement reviews; survey and questionnaire reviews; and Cooperative Research and Development Agreement (CRADA) and gift/grant (source, amount, and approval letter) reviews for the principal investigators (PI's) information only.

4.4.4.5. Serve as the Air Force Medical Service (AFMS) Continental United States (CONUS)/Outside CONUS (OCONUS) IRB of Record for clinical investigations and research involving human subjects for AF Medical Treatment Facilities without an internal IRB who seek an IAIR with the 59 MDW IRB.

4.4.4.6. Review and provide input into IRB OIs.

4.4.4.7. Bar use of data collected and prohibit publication of research without IRB approval.

4.4.5. New members and alternates to the 59 MDW IRB will receive orientation to their duties. All members must have a current certificate of training from the Collaborative

Institutional Training Initiative (CITI). CITI training can be accomplished on the CITI website at **http://www.citiprogram.org**. Re-current CITI training is every 3 years.

4.4.6. Research Monitor. For research involving greater-than-minimal risk to subjects, the 59 MDW IRB shall approve a Research Monitor (by name) who shall have the authority to temporarily suspend a research protocol in progress, remove individual subjects from a protocol, and take whatever steps are necessary to protect the safety and well-being of research subjects until the IRB can assess the Research Monitor's report.

4.5. 59 MDW Leadership. All 59 MDW leadership (e.g., Commanders, Directors, Division Chiefs, etc.) are responsible for the ethical and legal conduct of any research involving human subjects performed by their respective staff or Graduate Health and Science Education (GHSE) program students, including any resultant research publications or presentations submitted for approval. The department heads are responsible for attesting to: the soundness of the design of research protocols; the competency of the investigator(s) to conduct the project; and the presence of sufficient resources required for the research and for protecting research participant safety. Processes to support these assurances may include internal review committees or specialized review criteria within departments. If the PI fails to meet their responsibilities, the department head is the point of contact for correction of deficiencies.

4.6. 59 MDW PIs. PIs have the primary responsibility to safeguard the rights and welfare of each research subject. The PI will ensure compliance with applicable policies and procedures relating to the protection of human subjects and determinations of the 59 MDW IRB. The PI will also ensure that no undue influence will be asserted by any research team member towards any review or oversight committee, IRB member, or individuals involved with the 59 MDW HRPP.

4.6.1. Research Participant Requests for Information. The PI and members of the research staff are required to respond promptly and adequately to all requests for information received from participants, prospective participants, and their family members or designated representatives. Research personnel must also inform participants of how to contact the IRB if they have any questions about their rights as research subjects.

4.6.2. Research Participant Complaints. The PI is expected to investigate and respond promptly to complaints and to follow the proper procedure for addressing and reporting complaints to the IRB. Complaints that are not resolved promptly by the PI or a member of the research staff must be reported to the IRB. If the complaint is not directly related to the conduct or design of the research, the IRB staff may refer the complaint to the appropriate 59 MDW organizational official or committee. In circumstances in which the complaint is referred, the Office of Research Protocol Support staff should provide the participant with the name and contact information for the referral. On Continuing Review, investigators are required to list all complaints received about the research in the past year, whether or not they were previously reported to the IRB. Concerns and complaints of research participants are addressed by the IRB Clinical Research Administrator. Minor concerns/complaints are generally resolved by a phone call. More complex concerns/complaints are addressed by the IRB Clinical Research Administrator with the IRB Chair and others in the Office of Research Protocol Support. Participant

complaints may also be received directly by the Clinical Research Administrator (e.g., via email, phone) without going through the PI.

4.6.3. Research Investigator Questions, Comments, and Complaints. Research staff members and/or assigned personnel at the 59 MDW are encouraged to ask questions, provide process or research-related suggestions, and submit complaints to the Office of Research Protocol Support, IRB Clinical Research Administrator, IRB Chair, and/or the IO/AIO, as appropriate.

4.6.4. If the PI also holds an IND or IDE (Sponsor-Investigator), the additional responsibilities in overseeing the research normally assumed by sponsors in industry-sponsored projects apply. This includes the responsibility of registering all "applicable clinical trials" on the clinicaltrials.gov registry.

4.6.5. The PI is responsible for the handling and storage of all investigational devices approved for use in device studies involving human subjects.

4.7. Sponsors are the agencies, institutions, companies, organizations, foundations, or individual grantors responsible for the initiation, management, or financing of a research study. The term sponsor is understood to include any intermediaries, such as contract research organizations or coordinating centers, acting as agents of the sponsor in carrying out the responsibilities above. All research falling under these types of agreements is considered sponsored research. A sponsor is often, but not always, the entity that funds clinical research.

4.7.1. Special meaning in FDA-regulated research, the sponsor (i.e., IND or IDE holder) is the entity who takes responsibility for and initiates a clinical investigation. The sponsor can be any legal entity, including a company, an academic organization, or an individual. The intent of the sponsor's IND/IDE is to allow testing for marketing approval of the drug or device.

4.7.2. When collaborating with outside organizations who are sponsoring research involving human subjects (sponsors), the 59 MDW will ensure that contract or funding agreements:

4.7.2.1. Clarify who is responsible for medical care for research-related injury.

4.7.2.2. When the sponsor is responsible for monitoring the research (e.g., overseeing the progress), the sponsor or its agents should report findings of serious or continuing non-compliance detected during the monitoring process that could affect the safety of participants or influence the conduct of the study within 30 days.

4.7.2.3. When the sponsor is responsible for data and safety monitoring, the sponsor or its agents provides the reports from data and safety monitoring, including findings that emerge after the research has ended.

4.7.3. The Contract Specialist in coordination with the PI will ensure the following language is included in the statement of work or work plan sections of all non-DoD sponsored research agreements (e.g. Contracts, CRADAs):

4.7.3.1. The sponsor will provide payment to the institution for reasonable, unreimbursed medical expenses, including hospitalization, which the institution may incur as a direct result of the treatment of a subject's injuries that directly result from

the study drug or its administration during the clinical trial, as determined by the sponsor and the principal investigator.

4.7.3.2. The sponsor shall be responsible for payment of the actual and reasonable medical expenses incurred in diagnosing and treating any injury, illness, or adverse reaction of a study subject that results from the administration of the study drug or device in accordance with the protocol or the proper performance of any protocol procedure.

4.7.3.3. During and for a period of at least three years after the completion of the study, the sponsor shall promptly, within 30 days, report to the investigator any information that could directly affect the health or safety of past or current study subjects or influence the conduct of the study, including but not limited to the study results and information in site monitoring reports and data safety monitoring committee reports as required by the protocol. In each case, the investigator and the organization shall be free to communicate these findings to each study subject and the IRB.

4.8. 59 MDW HRPP Steering Committee. The HRPP Steering Committee is comprised of 59 MDW institutional components, DoD, and non-DoD (e.g., contractors) affiliated institutional representatives. The committee is charged with establishing procedures to integrate the 59 MDW HRPP institution-wide and to ensure the HRPP is maintained in accordance with, Federal, State, and local regulations, policies, and procedures. Committee meeting minutes are submitted to the 59 MDW Scientific Advisory Committee and then forwarded to the 59 MDW Board of Directors. Minutes represent feedback, comments, information, data, and action items discussed in the meeting. The committee also generates a "State of the HRPP" annual report for presentation to the IO/AIO that integrates quarterly programmatic assessments.

4.9. 59 MDW Office of the Chief Scientist. The Chief Scientist provides senior leadership and develops high-level collaboration among AF, DoD, local, national and international government, academic and industry, and development, test, evaluation and acquisition organizations. The Chief Scientist oversees and manages research activities of investigators at enterprise sites, the 59 MDW-San Antonio Military Medical Center (SAMMC), San Antonio Military Health System (SAMHS), DoD partners at the Battlefield Health and Trauma Research Institute and Tri-Service Research Laboratory, Joint Base San Antonio and the San Antonio Uniformed Services Health Education Consortium, Uniformed Services University of the Health Sciences and local universities to meet organizational needs, while leveraging medical research activities being funded by Congress as directed in the National Defense Authorization Act and meet the Secretary of Defense's mandate to develop tailored Research and Development investments. The 59 MDW Office of the Chief Scientist (59 MDW/ST), Science and Technology, supports commercialization and technology transfer activities (e.g., CRADAs), and provides centralized scientific, technical expertise and resources, project management, research and regulatory expertise to enable advancement of medical modernization to address mission capability gaps though the application of assistance, and direction and oversight to advance medical modernization through research. Knowledge gained from clinical studies and translational research is applied to create better health outcomes, improve readiness, enhance patient care, and advance capabilities across the Global Health System. The 59 MDW/ST provides 59 MDW staff and other AF, DoD and

non-DoD affiliated collaborative institutions (e.g., DoD Services, universities, civilian research organizations, etc.) expertise to enable/assist with performance of institutional, national, and international research to address Service and DoD specific scientific needs, AFMS top priorities and address warfighter and military beneficiary care mission capability gaps (e.g., as defined by Major Commands/Combatant Commands and Combat Support Agencies). The 59 MDW/ST also provides online training and education through SWANK on topics such as HRPP and Institutional and Research Conflict of Interest (COI) and disseminates printed information to investigators in the 59 MDW Research Resource Guide and various pamphlets. The 59 MDW/ST also provides oversight to any institutionally-designated Exempt Determination Officials (EDOs). EDOs are responsible for all Exempt and Non-Research/Not Human Research (NRNHR) determinations at the 59 MDW. EDOs route all non-exempt human research protocols to the Office of Research Protocol Support, and the Office of Research Protocol Support routes all Exempt and NRNHR activities to the EDOs. In the absence of EDOs, the 59 MDW IRB will assume the responsibility to make Exempt and NRNHR determinations at the 59 MDW.

4.10. 59 MDW Clinical Research Division, Office of the Chief Scientist. The 59 MDW Clinical Research Division (59 MDW/ST CRD), a subdivision of the 59 MDW/ST, supports Major Command-funded research, research involving human subjects, Graduate Medical Health Sciences Education scholarly activity, training of personnel involved in human subjects research, and the 59 MDW IRB through its Clinical Investigation Program (CIP), which is funded by Defense Health Program (DHP) operation and maintenance appropriated funds. The CIP is an essential component of medical care and teaching. The CRD CIP supports clinical investigation research for 59 MDW and SAMMC, SAMHS-assigned AF healthcare providers for the advancement and application of medical science for military and DoD beneficiary patient care. The CIP also supports operational health readiness training for GHSE students and other allied health programs. CIP DHP funds are intended to support USAF researchers with their IRB-approved GHSE and Clinical Investigations. Researchers requesting CIP funds must provide a copy of their IRB approval letter with their request for support. CIP funds cannot support any non-human/non-research or exempt activities or programs, other than non-exempt human subject research studies approved through IRB-designated reviewer determinations or the convened IRB (as required), regardless of any other federal policies that may be in effect. Based on the availability of CIP DHP funds, investigators can request funding for research publications that have been accepted by the publisher.

4.11. 59 MDW/ST CRD Compliance Office. The 59 MDW/ST CRD Compliance Office is responsible for developing and implementing of a Research Compliance Program providing oversight of human research through systematic audits. The Compliance Office maintains oversight to ensure adequacy of: communication with applicable committees, persons, and officials; documentation and reporting requirements of the auditing program; and adherence to timeframes for reporting and timelines for corrective actions required by the 59 MDW IRB.

4.12. 59 MDW Office of Public Affairs Oversight of Publications and Presentations. The Air Force is interested in fully informing the public about Air Force medical research activities. However, before such information is released to the public, it must be accounted for, reviewed, and cleared for security and consistency with Air Force, DoD, and federal

policies. The 59 MDW Office of Public Affairs provides security and policy reviews of all proposed publications, abstracts, and presentations for publication or dissemination in any public medium (e.g., public-facing HRPP webpage and HRPP "Tips of the Week" email bulletin announcements). These reviews facilitate coordination with other agencies (502 ISG/JAC, Air Education Training Command, Air Force Surgeon General's Office, etc.), as required. The 59 MDW/ST CRD maintains a computer database of all medical research publications, posters, and oral presentations cleared for public release.

4.13. 59 MDW Privacy Office. The 59 MDW Privacy Office ensures that approved research meets the HIPAA Privacy Rule and other regulatory requirements to protect the privacy of individually identifiable health information. The Privacy Office reviews each research protocol that is submitted to the 59 MDW IRB to ensure that legal authority exists prior to the use of Protected Health Information (PHI) and Personal Identifying Information (PII) for research and to ensure that legal authority exists prior to the disclosure of PHI/PII to outside entities for research purposes.

4.14. 59 MDW Office of the Judge Advocate. Where there is a question of applicability of federal, DoD, AF, and other research regulations and guidance, the 59 MDW Office of the Judge Advocate (59 MDW/JA) is consulted. The Medical Law Program ensures the Air Force has a cadre of trained personnel ready to provide medical law advice and support to medical centers, hospitals, and clinics, and to manage medical malpractice claims and litigation. Medical Legal Consultants advise the 59 MDW Commander and staff on all medical-legal matters including, but not limited to, release of medical information consistent with the Freedom of Information Act, the Privacy Rule, and the HIPAA of 1996 as it relates to patient care or research involving human subjects.

4.15. Office of Research and Technology Applications. The Air Force Medical Support Agency Surgeon General's Office of Research and Innovation (AFMSA/SG5), Office of Research and Technology Applications (ORTA) prepares application assessments for selected research and development projects in which a federal laboratory is engaged and which, in the opinion of the laboratory, may have potential commercial applications. ORTA provides and disseminates information on federally-owned or originated products, processes, and services having potential application to State and local governments and to private industry. ORTA cooperates with and assists the National Technical Information Service, the Federal Laboratory Consortium for Technology Transfer, and other organizations which link the research and development resources of that laboratory and the Federal Government as a whole to potential users in State and local government and private industry. ORTA participates, where feasible, in regional, State, and local programs designed to facilitate or stimulate the transfer of technology for the benefit of the region, State, or local jurisdiction in which the federal laboratory is located. ORTA is the focal point for clinical research technology transfer. ORTA supports translation of clinical research into practice, facilitates clinical researchers' collaborations with industry and academia, and enables AFMS PIs to reap benefits from research investments. Technology transfer is the exchange of knowledge, expertise, facilities, equipment, personnel, methods, technical information, and/or intellectual property.

4.16. 59 MDW Information Security Office. The 59 MDW Information Security Office ensures that all identifiable research data containing PHI/PII are collected, handled, and stored in a secure manner, as required by federal, DoD, and AF regulations. Examples of

how data are safeguarded include: providing and managing secured shared server folders for recordkeeping purposes (accessible only through specific computer permissions and Common Access Card (CAC) access; and by maintaining a CAC-accessible-only email server with options for marking emails for PII and For Official Use Only information with the added option for further encryption.

4.17. 59 MDW Pharmacy Flight. The 59 MDW Pharmacy Flight is responsible for implementation and monitoring of HRPP requirements associated with the use of investigational drugs. The pharmacy is involved in all phases of investigational drug studies, from planning through completion (e.g., receipt of drugs, storage, formulating, dispensing, etc.), and affords researchers adequate resources to support research studies. The pharmacy is the sole dispensary and storage location for all investigational drugs. Any issues or problems related to the safety and welfare of research subjects is reported IAW 21 CFR Part 312, 21 CFR Part 600, 59 MDWI 44-115, *Pharmacy and Medication Management*, and **https://www.citiprogram.org**.

4.18. 59 MDW Radiation Safety Committee. Research involving the use of radioactive substances or radiation, including standard of care procedures, must be approved by the Radiation Safety Committee (RSC) prior to IRB approval, on the basis of radiation protection standards and regulations. The RSC provides oversight of sources of radiation not covered by AFI 40-201, *Radioactive Materials (RAM) Management*, or AFI 91-108, *Air Force Nuclear Weapons Intrinsic Radiation and* 91(B), *Radioactive Material Safety Program*. The RSC priorities are: to ensure sources of radiation are operated in accordance with federal guidelines and AFIs; to review and approve research protocols using ionizing radiation; and to monitor status of internal and external inspections. The RSC reports its determinations on research involving the use of radiation to the IRB and immediately notifies the IRB, IRB Clinical Research Administrator, IO/AIO, and/or the IRB Chair of possible non-compliance with their determinations.

4.19. 59 MDW Scientific Ethics Subcommittee. The Scientific Ethics Subcommittee (SES), a component of the Scientific Advisory Committee, is responsible for reviewing research-related COI including individual investigator and institutional conflicts. The SES acts as the COI Committee for the 59 MDW. The COI Manager, staffed by the 59 MDW/ST, receives disclosure forms from researchers/research staff and reviews them for significant financial interest disclosures. If a disclosure meets the threshold for reporting, the form will be forwarded to the SES for determination. If the SES determines that a conflict(s) exists, the SES will work with the conflicted researcher to create a COI Management Plan. The Management Plan is approved by the IRB and IO/AIO, and filed with the COI Manager for tracking and compliance purposes. In addition, the SES annually reviews sources of institutional conflict and develops management plans as applicable.

5. Research Compliance and Oversight.

5.1. The IO/AIO will establish policies and procedures to foster integrity and unquestionable ethics in all human research activities consistent with applicable laws and regulations.

5.2. The IO/AIO shall respond to all allegations of non-compliance; research misconduct; and acts of intimidation, undue influence, coercion, and/or retaliation associated with human research protection requirements and/or the administration of IRB regulatory oversight of research involving human subjects and to ensure they are promptly reviewed and resolved

(e.g., corrective action plan). An IO/AIO-appointed investigation officer will be assigned to investigate all allegations.

5.3. Any individual, assigned personnel, patients, visitors or organizations involved in research at the 59 MDW may submit a written or verbal allegation of non-compliance, etc. Such submissions may be made to the IO/AIO, IRB Clinical Research Administrator, and/or the IRB Chair.

5.4. A climate free of fear of sanction is required to foster appropriate reporting and ensure a fair review of allegations. The 59 MDW shall take steps to protect individuals who make good faith allegations and their identities shall remain confidential to the extent possible. Retaliation against good faith "whistleblowers" is illegal and will not be tolerated.

5.5. If an investigation concludes that an allegation is valid, the IO or AIO shall promptly report the findings to: the IRB no later than 48 hours after discovery; to AFMSA/SGE-C (who shall notify the Assistant Secretary of Defense for Research and Engineering ASD (R&E), as applicable); to FDA or DHHS, as applicable; to other institutional commanders and appropriate funding agencies, as applicable.

6. Research Conducted Under the 59 MDW HRPP.

6.1. The 59 MDW HRPP covers all types of research involving human subjects conducted by personnel assigned to the 59 MDW under the 59 MDW DoD Assurance (50007):

6.1.1. Biomedical research.

6.1.2. Social and behavioral research.

6.1.3. Clinical investigation research.

6.1.4. Cancer clinical trials.

6.1.5. Clinical data research.

6.1.6. Data/tissue repository research.

7. Research Conducted/Not Conducted Under Special Conditions Under the 59 MDW HRPP.

7.1. Even if research activities meet the definition for research involving human subjects, not all categories of research are permitted under the 59 MDW HRPP or they may require special regulatory conditions to safeguard the rights and welfare of research subjects.

7.2. The 59 MDW HRPP does not normally permit the conduct of the following categories of research, however, under special circumstances, AFMSA/SGE-C and/or the Director of Defense Research and Engineering can approve these kinds of research, on a case-by-case basis, to be conducted under strict regulatory conditions:

7.2.1. Classified research.

7.2.2. Prisoner or detainee research.

7.2.3. Research conducted in a foreign country.

7.2.4. Fetal research.

7.2.5. Research involving biological or chemical warfare agents or weapons.

8. Activities That May or May Not be Human Research.

8.1. The AF authorizes only AFMSA/SGE-C, IRBs, and EDOs to make official determinations regarding whether activities are not research involving human subjects, exempt research involving human subjects, or research involving human subjects that requires IRB approval prior to initiation.

8.2. AFMSA/SGE-C Guidance Memorandum 2016-0002G. *Guidance on Activities That May Be Research Involving Human Subjects*, clarifies that the activities listed in Part II of the Glossary (under "*Research Involving Human Subjects*") will not require an official determination if they will be conducted exactly as characterized, and the data/specimens from the activity will not be used in any way other than to support the primary aim identified in each activity's definition.

9. Education and Training.

9.1. All DoD personnel at the 59 MDW are required to receive initial and continuing human subjects protection education and training commensurate with their duties and responsibilities. The 59 MDW/ST provides online training and education through SWANK on topics of HRPP and Institutional and Research Conflict of Interest (COI). The HRPP and COI training will be tracked by the Office of the Chief Scientist

9.2. Each PI who submits a human research protocol for review by the 59 MDW IRB is required to complete the University of Miami web-based CITI program in human subjects protection. All research team members listed on the protocol and research monitors (if required) must also complete CITI training. Documentation of CITI training must be received before final IRB approval is granted for the study. This is one of several ways that the IRB ensures that investigators possess the appropriate knowledge and skills required to conduct research protocols.

9.3. The basic CITI course may be accessed and completed at: **http://www.citiprogram.org/**. The 59 MDW Office of Research Protocol Support may be contacted for additional assistance.

9.3.1. The following training groups may be selected and completed, as required:

9.3.1.1. Group 1 – Biomedical research with human subjects.

9.3.1.2. Group 2 – Exempt biomedical research with human subjects.

9.3.1.3. Group 3 – Social/humanistic/behavioral research with human subjects.

9.3.1.4. Group 4 – Exempt social/humanistic/behavioral research with human subjects.

9.3.2. A passing score of 80 percent for each module and an overall passing score of 80 percent for the entire course is required. The CITI course transcript should be downloaded and retained for your records. The Office of Research Protocol Support will automatically receive notification that the training is complete.

9.3.3. CITI training is valid for 3 years from the initial training date and must be renewed by taking the CITI Refresher Course. If an investigator's CITI training expires, they must be removed from the research study until the training is re-accomplished. If the PI's CITI training expires, the 59 MDW IRB may make a determination to suspend the

research until the PI re-accomplishes the training. The 59 MDW IRB may not approve a Continuing Review Report or amendment to a study if the PI's training is not current. If a request is made to change the PI, the 59 MDW IRB may not approve the change if the new PI does not have current CITI training.

9.3.4. The 59 MDW Office of Research Protocol Support will accept from any engaged DoD institution HRPP training certificate documenting compliance with standards set forth by ASD (R&E).

9.3.5. For FDA-regulated research, the PI is required to complete Good Clinical Practice (GCP) training on the CITI training website every three (3) years. Completion of GCP training is optional for other research team members. The pass rate is 80 percent. The Office of Research Protocol Support automatically receives notification that training is complete for verification purposes during administrative review.

9.3.6. COI training is required for anyone who is responsible for the design, conduct, or reporting of research involving human subjects at the 59 MDW. Significant financial interests related to research must be disclosed at least annually.

10. Continuity of Operations Strategy.

10.1. Air Force has developed an HRPP Continuity of Operation Strategy in order to maintain HRPP operations in the event of government closure, whether temporary, prolonged, local, partial (e.g., furlough for some) or national as the result of weather, appropriation lapse, or other national disaster event resulting in a forced reduction in HRPP personnel. The purpose of this Strategy is to ensure the safety, rights, and welfare of participants in Air Force programs subject to 32 CFR 219 ("the Common Rule") and DoDI 3216.02_AFI 40-402.

10.2. For short term closures, Air Force shall deem essential one HRPP government staff member at AFMSA/SGE-C and each of the 6 Air Force IRBs with appropriate experience and authority to continue to carry on duties (e.g., Institutional Review Board (IRB) functions, Human Research Protection Official functions, reporting of unanticipated problems, non-compliance). If not possible to maintain staffing, HRPP offices may refer customers to an alternate HRPP office. Non-DoD institutions conducting AF supported human research and subjects in Air Force conducted human research must be provided appropriate alternate HRPP contacts. If the PI or research monitor is furloughed without an alternate, the research must stop until this duty resumes. Every Air Force protocol shall be covered by a contingency plan. If protocol deviations are necessary to ensure subject safety and/or welfare, the PI should get prior IRB approval; if not possible, these shall be reported to the IRB immediately. IOs must assess whether any ongoing research can continue or must stop.

10.3. For long term closures affecting AFMSA/SGE-C, remaining staff (or, if no staff remain, AFMSA/SGE-C's alternate HRPP official) shall report to AF/SG whether staffing is sufficient to oversee the AF HRPP, and appropriate courses of action; AF/SG shall determine the appropriate way forward. For long term closures affecting local Air Force institutions, Institutional Officials (IOs) shall report to AFMSA/SGE-C their plan of action and HRPP status; AFMSA/SGE-C assesses the plan and responds accordingly (e.g., via

acknowledgment with no action necessary, request for additional corrective action, or suspension of the institution's assurance).

SCOTT C. SUCKOW, Colonel, USAF, MSC
Administrator

Attachment 1

GLOSSARY OF REFERENCES AND SUPPORTING INFORMATION

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Adopted Form

AF Form 847, *Recommendation for Change of Publication*

Abbreviations and Acronyms

AF—Air Force
AFMS—Air Force Medical Service
AFMSA—Air Force Medical Support Agency
AIO—Authorized Institutional Official
CAC—Common Access Card
CIP—Clinical Investigation Program
CITI—Collaborative Institutional Training Initiative
COI—Conflict of Interest
CONUS—Continental United States
CRADA—Cooperative Research and Development Agreement
DHHS—Department of Health and Human Services
DHP—Defense Health Program
DoD—Department of Defense
EDO—Exempt Determination Official
FDA—Food and Drug Administration
GCP—Good Clinical Practice
GHSE—Graduate Health and Science Education
HIPAA—Health Insurance Portability and Accountability Act
HRPP—Human Research Protection Program
IAW—In Accordance With
IAIR—Institutional Agreement for IRB Review
IDE—Investigational Device Exemptions
IND—Investigational New Drug
IO—Institutional Official
IRB—Institutional Review Board
FWA—Federal Wide Assurance
MDW—Medical Wing
MDWI—Medical Wing Instruction
NRNHR—Non-Research/Not Human Research
OCONUS—Outside CONUS
OHRP—Office of Human Research Protection
OI—Operating Instruction
ORTA—Office of Research and Technology Applications
PHI—Protected Health Information
PI—Principal Investigator
PII—Personal Identifying Information
R&E—Research and Engineering
RSC—Radiation Safety Committee
SAMHS—San Antonio Military Health System
SAMMC—San Antonio Military Medical Center
SES—Scientific Ethics Subcommittee
UPIRSO—Unanticipated Problems Involving Risk to Subjects or Others
USC—United States Code