

**BY ORDER OF THE COMMANDER
59TH MEDICAL WING**

**59TH MEDICAL WING INSTRUCTION
40-403**



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Medical Command

**HUMAN RESEARCH PARTICIPANT
AND ANIMAL SUBJECT PROTECTION,
QUALITY ASSURANCE/QUALITY
IMPROVEMENT**

COMPLIANCE WITH THIS PUBLICATION IS MANDATORY

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This instruction implements Air Force Policy Directive 40-4, *Clinical Investigation and Human Use in Medical Research*. This instruction establishes policy and procedures for the implementation and execution of the Quality Assurance/Quality Improvement (QA/QI) activities supporting clinical investigations conducted by personnel assigned to the 59th Medical Wing (59 MDW). This instruction does not apply to the Air National Guard or Air Force Reserve. Refer recommended changes and questions about this publication to the Office of Primary Responsibility using the AF Form 847, *Recommendation for Change of Publication*. The authority to waive requirements is the publication approval authority. Ensure that all records created as a result of processes prescribed in this publication are maintained IAW Air Force Manual 33-363, *Management of Records*, and disposed of IAW Air Force Records Information Management System Records Disposition Schedule.

SUMMARY OF CHANGES

This publication has been revised. This rewrite of 59 MDWI 40-403 includes updated governing QA/QI principles.

1. Purpose.

1.1. Human and animal research subject protection QA/QI is a service provided by the 59 MDW Clinical Research Division (CRD) as part of research support by the Clinical

Investigation Program as described in DoDI 6000.08, *Defense Health Program Research and Clinical Investigation Programs*. The purpose of this instruction is to delineate the purpose, principles, functions, and operations of CRD QA/QI Support Staff. This instruction specifically pertains to research involving the use of human subjects not exempt from 59 MDW Institutional Review Board (IRB) review, as described by 32 CFR 219, *Protection of Human Subjects*, 21 CFR 56, *Institutional Review Boards*, and DoDI 3216.02_AFI 40-402, *Protection of Human Subjects and Adherence to Ethical Standards in Air Force Supported Research* and the use of animal subjects not exempt from 59 MDW Institutional Animal Care and Use Committee (IACUC) review, as described by *The Animal Welfare Act of 1966* (P.L. 89-544), 29 CFR 1910.1450, *Occupational Exposure to Hazardous Chemicals In Laboratories*, DoDI 3216.02, *Protection of Human Subjects and Adherence to Ethical Standards in DoD Supported Research*, AFMAN_IP 40-401, *The Care and Use of Laboratory Animals in DoD Programs*, and *The Guide for the Care and Use of Laboratory Animals* (NRC 2011). The mission of CRD QA/QI Support Staff is to perform post-approval monitoring (PAM) to identify regulatory non-compliance and help protect the rights and welfare of human and animal research subjects recruited to participate in research studies at the 59 MDW, under the 59 MDW Federal-wide Assurance and Department of Defense (DoD) Assurance, by:

- 1.2. Ensuring compliance with DoD policies and federal rules and regulations;
- 1.3. Identifying education/training initiatives for investigators, research staff, and others; and
- 1.4. Assisting in obtaining and maintaining accreditation for research programs that involve the:
 - 1.4.1. Protection of human subjects in research.
 - 1.4.2. Use of animals by the 59 MDW.
- 1.5. Promoting a working relationship among investigators, research staff, applicable oversight Committee (e.g., IRB; IACUC), and CRD QA/QI Support Staff.

2. Principles Governing QA/QI.

2.1. QA/QI is comprised of three basic components, as identified by the Office for Human Research Protections Division of Assurances and Quality Improvement, and satisfies requirements for PAM as provided in *The Guide for the Care and Use of Laboratory Animals* (NRC 2011, pages 33-34):

- 2.1.1. Quality Assurance. Assessing strengths and weaknesses through internal and external self-assessments and/or program evaluations intended to gauge compliance and evaluate known or suspected problems.
- 2.1.2. Quality Improvement. Based on QA activities, QI establishes mechanisms, processes, and relationships that extend beyond compliance in order to improve the quality of internal and external activities.
- 2.1.3. Continuous Quality Improvement. An open and flexible environment for self-evaluation and improvement in internal and external activities.
 - 2.1.3.1. Internal activities include 59 MDW IRB/IACUC operations and support activities.

2.1.3.2. External activities include investigator activities.

2.2. PAM Monitor Activities:

2.2.1. For-Cause (requested) research protocol audits and site visits (internal/external).

2.2.2. Random research protocol audits and site visits (internal/external).

2.2.3. Continuous Education for Quality Assurance.

2.3. Role of the PAM Monitor. The PAM Monitor arranges and performs monitoring visits (on-site and off-site), performs protocol reviews or reviews of the consent process, and oversees the continuous education for quality assurance in research at the 59 MDW. The PAM Monitor:

2.3.1. Reports directly to the CRD director;

2.3.2. Prepares an annual plan for the oversight of 59 MDW IRB/IACUC protocol audits/site visits, facilitates formal investigations, and conducts IRB/IACUC research continuing education;

2.3.3. Directs and conducts Internal and External QA/QI activities as directed by: 59 MDW IRB, 59 MDW IACUC, Institutional Official (IO) of the animal program, IO/Authorized Institutional Official (AIO) of the Human Research Protection Program (HRPP), and/or HRPP Steering Committee for protocol(s) requiring follow-up.

2.3.4. Access to Documents, Records and Staff. The PAM Monitor shall have access to all documents and information maintained by the investigator and/or applicable oversight committee (IRB/IACUC) as part of any For-Cause protocol audits/site visits or Random protocol audits/site visits. The PAM Monitor shall have access to any research staff, committee members, or committee oversight staff to conduct interviews as part of any audit/site visit.

2.3.5. PAM Monitor's Report. The PAM Monitor will submit a report of his/her findings to the IRB/IACUC, the investigator, the IO for the animal program, and the IO/AIO for the HRPP, as detailed in section 3.1 below. The report will list any identified violations or areas of research non-compliance or scientific misconduct and include the basis and background of the violations and/or areas of non-compliance. The report, where appropriate, shall list areas that demonstrate quality research compliance and provide recommendations for quality and/or compliance improvement.

2.3.6. Records, gathers data, collates, and compiles the following HRPP QA/QI activity data and presents annually to the HRPP Steering Committee:

2.3.6.1. IRB Turnaround Times (TAT);

2.3.6.2. Evaluation of IRB Customer Satisfaction Surveys;

2.3.6.3. PAM Auditing Metrics (Investigator/IRB Record);

2.3.6.4. IRB-related Process Improvements.

3. Relationships.

3.1. 59 MDW IRB/IACUC:

3.1.1. Reviews, discusses, and documents PAM Reports at convened meetings and provides evaluation and feedback on compliance and improvement opportunities;

3.1.2. Directs and evaluates improvement initiatives recommended by the 59 MDW IRB/IACUC, based on evaluation and feedback;

3.1.3. 59 MDW IRB provides annual review and feedback on Food and Drug Administration compliance of selected investigational drug and device studies;

3.1.4. Forwards copies of PAM Reports to the IO for the animal program and the IO/AIO for the HRPP following IRB/IACUC review and discussion;

3.1.5. Reviews and approves HRPP QA/QI activity data for presentation to the HRPP Steering Committee.

3.2. The PAM Monitor provides evaluation and feedback on compliance and improvement opportunities through the following post-approval monitoring tools:

3.2.1. Monitoring IRB/IACUC-approved research through the continuing review process and other required reporting processes;

3.2.2. Random (No-Cause) Protocol Audits/Site Visits: Random protocol audits/site visits are scheduled and conducted by the PAM Monitor or may be requested by the principal investigator/research staff. These audits tend to take on the dual role of assisting with identifying issues, resolving them, and providing continuing education. They will be conducted on an ongoing basis. PAM records and reports are retained IAW AFMAN 33-363. The primary emphasis for these audits will include human use protocols involving greater-than-minimal risk and/or involving vulnerable populations, non-exempt animal research and training studies or unique circumstances. Outcomes of the audits/site visits will be provided in writing to the 59 MDW IRB/IACUC Chairs, IO of the animal program, IO/AIO of the HRPP, and HRPP Steering Committee, as detailed in section 3.1, and discussed and documented at convened 59 MDW IRB/IACUC meetings.

3.2.3. Requested (For-Cause) Protocol Audits/Site Visits: Requested for-cause protocol audits/site visits are scheduled by the PAM Monitor at the request of the: IO/AIO of the HRPP; IO of the animal program; and 59 MDW IRB/IACUC. These audits/visits will include a formal audit and reporting component. This activity may include direct audits of study records at the study site, contact with the research sponsor and/or monitoring organizations, contact with other IRBs, interviews with research staff and research participants, and/or review of 59 MDW Office of Research Protocol Support IRB/IACUC records.

3.2.4. Outcomes of the monitoring visit will be made available to the 59 MDW IRB/IACUC Chairs, IO/AIO of the HRPP, and IO of the animal program, as detailed in section 3.1. Records and reports are retained by the PAM Monitor IAW AFMAN 33-363. Any 59 MDW IRB/IACUC-approved protocol may be subject to a requested protocol audit/site visit.

3.2.5. The 59 MDW IRB may request monitoring of the consent process at any time. Factors that may prompt Consent Observation include any specific complaint or concern raised that relates or may relate to the consent process.

3.2.6. The PAM Monitor directs and evaluates improvement initiatives recommended by the 59 MDW IRB/IACUC based on evaluation and feedback from PAM tools.

3.3. Research Investigators:

3.3.1. Provide evaluation and feedback on compliance and improvement opportunities.

3.3.1.1. Anonymously through self-evaluation programs.

3.3.1.2. During for-cause evaluations, as directed by the 59 MDW IRB/IACUC, IO/AIO of the HRPP, and IO of the animal program.

3.3.2. Implement compliance and improvement recommendations or directives.

4. Duties and Responsibilities of the Principal Investigator and Research Staff.

4.1. The Principal Investigator and/or Oversight Committee Chair or their designees shall meet with the PAM Monitor at the beginning of any Requested (For-cause) Protocol Audits/Site Visits or Random (No-cause) Protocol Audits/Site Visits to answer any questions. The principal investigator shall receive a copy of the PAM Monitor's report as it relates to his/her research protocol.

4.2. The investigator will comply with all requirements of this Instruction.

4.3. The investigator will comply with all requests for an audit/PAM assessment and any stipulations required by any QA/QI audit report or post-approval monitoring assessment.

4.4. Failure to comply with a request for an audit and any stipulations of an audit will result in notification being sent to the IRB and/or IACUC, and may result in administrative actions and/or sanctions, up to and including possible legal action IAW DoDI 3210.7, *Research Integrity and Misconduct* and 59 MDWI 40-401, *Research Misconduct*.

5. Continuing Education for Quality Assurance.

5.1. Principal Investigator (PI) Self-Assessment Program. The PI Self-Assessment Program is a tool for human and animal research investigators to use in an effort to effect quality improvement at the study-site level and enhance continuing education of investigators. It is designed for use by both biomedical and social science researchers and focuses upon issues regarding quality documentation and recordkeeping consistent with managing overall IRB compliance (for non-exempt IRB-approved protocols) and IACUC compliance. The goal of the PI Self-Assessment Program is to improve quality by identifying issues that may have come up during the IRB or IACUC review cycle and reporting them promptly to the 59 MDW IRB or IACUC. Specific uses by the investigator and/or research staff include: (a) training new research personnel; (b) preparing for 59 MDW, sponsor, or regulatory agency site visits; or (c) a routine quality improvement exercise.

5.2. Research Education. Research education already exists at the 59 MDW and is offered to Principal Investigators and/or Research Personnel as outlined in 59 MDWI 41-105, *59 MDW Human Research Protection Program* and 59 MDW IACUC Policy 2016-23, *Policy on Training of Personnel Associated with the Animal Care and Use Program*. The PAM

Monitor may offer additional, voluntary programs or seminars to discuss topics in research compliance or research quality improvement.

JOSEPH R RICHARDS, Colonel, USAF, MC
Chief of the Medical Staff

Attachment 1**GLOSSARY OF REFERENCES AND SUPPORTING INFORMATION*****References***

AFPD 40-4, *Clinical Investigation and Human Use in Medical Research*, 11 May 1994

DoDI 6000.08, *Defense Health Program Research and Clinical Investigation Programs*, 22 January 2014

Title 32, Code of Federal Regulations, Part 219, *Protection of Human Subjects*, 1 July 2015

Title 21 Code of Federal Regulations, Part 56, *Institutional Review Boards*, 1 April 2016

29 CFR 1910.1450, *Occupational Exposure to Hazardous Chemicals In Laboratories*, 1 September 2016

DoDI 3216.02_AFI 40-402, *Protection of Human Subjects and Adherence to Ethical Standards in Air Force Supported Research*, 10 September 2014

The Animal Welfare Act of 1966

Title 29 Code of Federal Regulations, Section 1910.1450, *Occupational Exposure to Hazardous Chemicals In Laboratories*, 1 July 2015

DoDI 3216.01, *Protection of Human Subjects and Adherence to Ethical Standards in DoD Supported Research*, 8 November 2011

AFMAN_IP 40-401, *The Care and Use of Laboratory Animals in DoD Programs*, 16 February 2005

The Guide for the Care and Use of Laboratory Animals, NRC 2011

AFMAN 33-363, *Management of Records*, 1 March 2008

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

59 MDWI 40-401, *Research Misconduct*, 14 July 2016

59 MDW IACUC Policy 2016-23, *Policy on Training of Personnel Associated with the Animal Care and Use Program*

Adopted Form

AF Form 847, *Recommendation for Change of Publication*

Abbreviations and Acronyms

59 MDW—59th Medical Wing

AIO—Authorized Institutional Official

CRD—Clinical Research Division

DoD—Department of Defense

HRPP—Human Research Protection Program

IACUC—Institutional Animal Care and Use Committee

IAW—In Accordance With

IO—Institutional Official

IRB—Institutional Review Board

PAM—Post-Approval Monitoring

PI—Principal Investigator

QA—Quality Assurance

QI—Quality Improvement