



**Walter Reed Army Institute of Research
Standard Operating Procedure**



SOP Title:	REPORTING REQUIREMENTS TO USAMRMC ORP HRPO FOR HEADQUARTERS - LEVEL REVIEW AND TO AHRPO	SOP No. UWZ-C-636
		Version .02
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Signatures and

Author:

QA Director:

For signatures, please see original in the
Division of Human Subjects Protection

WRAIR IRB
Administrative
Director:

Change Control: Review/Approval for unchanged documents

Date	Author	QA Review	Approving Authority



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1. Purpose/Applicability:

This Standard Operating Procedure (SOP) summarizes the current reporting requirements of the United States Army Medical Research and Materiel Command's (USAMRMC) headquarters-level and the Army Human Research and Protection Office (AHRPO), and outlines the processes for ensuring compliance with those requirements by the Walter Reed Army Institute of Research (WRAIR) Institutional Review Board (IRB), WRAIR Division of Human Subjects Protection (DHSP), and the Institutional Official (IO).

This SOP applies to the WRAIR IRB Chair or designee, WRAIR IRB, the WRAIR IRB Administrator, the Division of Human Subjects Protection staff, and the IO.

2. Background:

As described in the WRAIR Human Research Protection Program (HRPP), headquarters (HQ)-level oversight of the WRAIR HRPP is provided by the USAMRMC Office of Research Protections (ORP), Human Research Protection Office (HRPO).

Historically, certain protocol lifecycle activities have required the investigator to report directly to USAMRMC ORP HRPO, bypassing, or in parallel to, reporting to the WRAIR IRB/DHSP. This SOP defines a change in practice, whereby these lifecycle actions will be reported to the USAMRMC ORP HRPO by the DHSP. The IO has delegated his reporting responsibilities to the DHSP for all actions requiring reporting to USAMRMC ORP HRPO and/or AHRPO.

3. Responsibilities:

a. WRAIR DHSP staff are responsible for:

- 1) Receiving telephone, email, facsimile, and/or written reports for protocol deviations, unanticipated problems, noncompliance issues, serious adverse events (SAEs), suspensions, clinical holds, study terminations, and knowledge of any pending compliance inspection/visit by the FDA, OHRP, or other government agency concerning clinical investigations or research.
- 2) Assessing and distributing deviation and unanticipated problem reports to the WRAIR IRB Chair or designee for review as per SOP UWZ-C-621, "Deviation and Unanticipated Problem Reporting for Human Subjects Research Protocols."



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- 3) Assessing and distributing related SAE reports to the WRAIR IRB Chair/designee for review as per SOP UWZ-C-619, "Safety Reporting for Clinical Trials."
 - 4) Assessing and distributing noncompliance issues to the WRAIR IRB Chair/designee for review as per SOP UWZ-C-606, "Noncompliance Procedures."
 - 5) Reporting suspensions, clinical holds, study terminations, and knowledge of any pending compliance inspection visit by the FDA, OHRP, or other government agency concerning clinical investigations or research to the WRAIR IRB Chair or designee.
 - 6) Receiving and conducting an initial review of protocol amendments as per UWZ-C-615, "Amendments to Human Subjects Research Protocols," and submitting them to the WRAIR IRB Chair or designee for review.
 - 7) Receiving and conducting an initial review of continuing review reports as per UWZ-C-618, "Continuing Review and Continuation Determination," and submitting them to the WRAIR IRB Chair or designee for review.
 - 8) Notifying USAMRMC ORP HRPO and providing supporting documentation, as required in USAMRMC ORP HRPO study approval memoranda and protocol reporting requirements, as described in this document, and as directed by the WRAIR IRB Chair or designee, and/or WRAIR IRB.
 - 9) Notifying AHRPO of unanticipated problems involving risks to subjects or others, serious or continuing noncompliance, suspensions, and study terminations, on behalf of the IO, and providing supporting documentation.
 - 10) Archiving all acknowledgement and acceptance memoranda received from the USAMRMC ORP HRPO with the appropriate protocol action.
 - 11) Forwarding WRAIR IRB Monthly Meeting Minutes to USAMRMC ORP HRPO, upon receipt of final, official signatures.
- b. The WRAIR IRB Chair or designee is responsible for:
- 1) Initial IRB review and assessment of deviations, unanticipated problems, SAEs, and noncompliance issues.



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- 2) Initial IRB review and assessment of amendments and continuing review reports.
 - 3) Recommending initial action on behalf of the IRB and referring the protocol actions to the WRAIR IRB, as appropriate, for review.
- c. The WRAIR IRB is responsible for:
- 1) Reviewing protocol life-cycle events (e.g., continuing reviews) and other protocol events reported to the IRB (e.g., unanticipated problems involving risks to subjects or others) and making determinations in accordance with IRB policies and SOPs.
 - 2) Reviewing modifications to currently approved research protocols and referring those proposed modifications that may increase risks to subjects or others to the USAMRMC ORP HRPO prior to implementation.
 - 3) Reviewing and referring to the USAMRMC ORP HRPO modifications to currently approved research protocols initially approved as minimal risk but now present greater than minimal risk.
- d. The WRAIR IO is responsible for ensuring reporting is done in compliance with all applicable regulations, policies and laws.

4. Reporting Requirements to USAMRMC ORP HRPO:

- a. The following events must be promptly (within 10 working days of being notified) reported to the USAMRMC ORP HRPO for all research in which the WRAIR is engaged:
- 1) All instances of noncompliance determined to be serious and/or continuing by the IRB;
 - 2) Any allegation of noncompliance that is potentially serious or continuing noncompliance based on the gravity or magnitude of the initial allegation (i.e., possible public disclosure of an event, subject; injury);
 - 3) All institutional noncompliance;
 - 4) Noncompliance involving a potential conflict of interest among the IRB members or Institutional Official, or if an allegation of noncompliance cannot be investigated adequately regardless of the reason;



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- 5) All suspensions, clinical holds (voluntary or involuntary), or terminations of the research by the IRB, the institution, the Sponsor, or regulatory agencies are to be promptly reported to the USAMRMC ORP HRPO.
 - 6) The knowledge of any pending compliance inspection/visit by the FDA, OHRP, or other government agency concerning clinical investigation or research, the issuance of Inspection Reports, FDA Form 483, warning letters or actions taken by any Regulatory Agencies including legal or medical actions and any instances of serious or continuing noncompliance with the regulations or requirements are reported immediately to USAMRMC ORP HRPO.
- b. The following protocol life-cycle actions must be promptly (within 10 working days of being notified) reported to the USAMRMC ORP HRPO for all research in which the WRAIR is engaged:
- 1) All unanticipated problems involving risk to subjects or others, all serious adverse events related to participation in the study and all subject deaths related to participation in the study.
 - 2) Any deviation to the protocol that may have an adverse effect on the safety or rights of the subjects or the integrity of the study must be reported to the USAMRMC ORP HRPO as soon as the deviation is reported to the DHSP.
 - 3) Any modification (amendment) to a research protocol previously reviewed by USAMRMC ORP HRPO that may increase risk to subjects or any to a protocol initially approved as minimal risk but that is subsequently determined by the WRAIR IRB to present greater than minimal risk must be submitted to the USAMRMC ORP HRPO prior to implementation.
- c. The following protocol lifecycle actions initially reviewed by the WRAIR IRB require periodic reporting for HQ-level review by the USAMRMC ORP HRPO.
- 1) Modifications (amendments) to the research protocol which do not increase risk to subjects must be submitted to the WRAIR IRB Chair or designee or the WRAIR IRB, as appropriate, for review and approval. These amendments are submitted to the USAMRMC ORP HRPO after implementation.



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- 2) A copy of the approved continuing review report, supporting documentation (to include protocol, consent, IRB approvals from engaged institutions), and the WRAIR IRB acceptance memorandum are submitted to the USAMRMC ORP HRPO as soon as these documents become available.
- 3) A copy of the approved closure study report, WRAIR IRB acceptance memorandum, and local IRB approval(s) will be submitted to the USAMRMC ORP HRPO as soon as these documents become available.
- 4) WRAIR IRB Monthly Meeting Minutes are sent to USAMRMC ORP HRPO upon receipt of final, official signatures. Reporting to the USAMRMC ORP HRPO may be accomplished by email (HSRRB@amedd.army.mil), or through the US mail to the U.S. Army Medical Research and Materiel Command, ATTN: MCMR-RP, 504 Scott Street, Fort Detrick, Maryland 21702-5012.

5. Procedures for ensuring reporting to the USAMRMC ORP HRPO:

- a. The WRAIR DHSP and IRB have developed policies to define investigator reporting requirements of unanticipated problems involving risk to subjects or others, serious adverse events related to participation in the study, subject deaths, and major deviations. These are defined in various policies and SOPs on the WRAIR DHSP website at www.wrairdhsp.com.
- b. It is WRAIR IRB policy that these reporting requirements are articulated in template language for IRB reporting requirements and inserted, as appropriate, in all protocols reviewed by the WRAIR IRB.
- c. Once the protocol action is received from the principal investigator (PI) to the DHSP mailbox (WRAIRDHSP@amedd.army.mil) or in person, the protocol action is then routed to the appropriate human subject protection scientist, logged into the IRB regulatory file, and the routing coversheet is added, as appropriate. Once an initial DHSP assessment has been conducted, the protocol action is then forwarded to the IRB Chair or designee for review and to the USAMRMC ORP HRPO as appropriate.
- d. The IRB Chair or designee reviews the protocol and/or event and determines the immediate course of action, to include review by the WRAIR IRB and notification to the USAMRMC ORP HRPO if not yet notified.



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6. Procedures and Reporting Requirements for AHRPO

- a. The following events must be reported to AHRPO for all research in which the WRAIR is engaged:
 - 1) All instances of noncompliance determined to be serious and/or continuing by the IRB;
 - 2) All suspensions or terminations of the research by the IRB, the institution, the Sponsor, or regulatory agencies;
 - 3) Unanticipated Problems determined by the WRAIR IRB to Involve Risks to Subjects or Others.
- b. These events are reported to the IO by the WRAIR DHSP.
- c. Upon notification of these events, the IO requests that the WRAIR DHSP report these events to AHRPO on his behalf.
- d. Reporting to AHRPO may be accomplished by email (fabian.sandoval1@us.army.mil) or through the U.S. mail as follows: Army Human Research Protections Office, Office of The Surgeon, 2511 Jefferson Davis Highway, Room 11200, Arlington, VA 22202

7. Extramurally-Funded Projects:

- a. For projects that receive funding from extramural sources (e.g., The Henry M. Jackson Foundation) upon receipt of the protocol, the DHSP will ensure the USAMRMC ORP HRPO receives all study documents in order to conduct the necessary headquarters-level review regardless of the IRB's determination of the WRAIR engagement or study risk level. This may be accomplished by sending the project documents to the USAMRMC ORP HRPO or by notifying the USAMRMC ORP HRPO that they should work directly with the funders during the headquarters-level review process.
- b. The exception to this is when the award agreement (i.e., contract or cooperative agreement) specifically allows for the WRAIR to conduct headquarters-level review without USAMRMC ORP HRPO oversight.

8. Transition Plan for Currently Approved Protocols

- a. All active protocols currently approved by the WRAIR IRB continue to follow the protocol lifecycle reporting language in the currently approved protocol. Hence, protocols that currently have language requiring direct reporting to USAMRMC ORP HRPO continue to do so.



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- b. At the time of any planned amendment or continuing review, reporting language to the USAMRMC ORP HRPO is to be updated IAW the guidance herein, unless the USAMRMC ORP HRPO requires different reporting on a per-protocol basis.. If the protocol includes language referencing the Human Subjects Research Review Board (HSRRB) the protocol will be updated to replace references to the HSRRB with USAMRMC ORP HRPO (note that the email address for still contains the name HSRRB).



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9. Explanation of Abbreviations and Terms:

AHRPO	Army Human Research Protection Office
DHSP	Division of Human Subjects Protection, WRAIR, is the administrative support for the WRAIR IRB.
FDA	Food and Drug Administration
HQ	Headquarters
HRPP	Human Research Protection Program
IO	Institutional Official
PI	Principal Investigator or WRAIR POC
POC	Point of Contact
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
USAMRMC ORP HRPO	U.S. Army Medical Research and Materiel Command, Office of Research Protection, Human Research Protection Office
WRAIR	Walter Reed Army Institute of Research
WRAIR Institutional Review Board (IRB)	WRAIR Institutional Review Board, the ethical review committee, for research involving human subjects at WRAIR, Its CONUS detachments or Overseas Laboratories, or when WRAIR funding, facilities or personnel are involved in any way (i.e., investigator). This includes protocols for which recruitment of subjects is through WRAIR.



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10. References:

Reference Number or Authors	Document Title
32 Code of Federal Regulations	Protection of Human Subjects, 18 June 1991
DoD Directive 3216.02	Protection of Human Subjects and Adherence to Ethical Standards in DOD-Supported Research, 24 April 2007
AR-70-25	Use of Volunteers as Subjects of Research, 25 January 1990
USAMRMC Command Policy 2010-03	Investigating, Managing and Reporting Non-compliance with Human Subjects Research Regulatory Requirements for US Army Medical Research and Materiel Command (USAMRMC) Intramural Research
USAMRMC Command Policy 2011-67	Reporting Suspensions or Terminations of Institutional Review Board (IRB) Approval and Unanticipated Problems Involving Risks to Subjects or Others (UPIRTSOs) in Human Subjects Research Conducted or Supported by the U.S. Army Medical Research and Materiel Command (USAMRMC)
United States Army Medical Research and Materiel Command Office of Research Protections (ORP)	Human Research Protection Office Policies & Procedures
WRAIR HRPP	WRAIR Human Research Protection Program (HRPP)
WRAIR IRB Charter	Walter Reed Army Institute of Research Institutional Review Board (WRAIR IRB) Charter
UWZ-C-618	Continuing Review and Continuation Determination
UWZ-C-606	Noncompliance Procedures
UWZ-C-615	Amendments to Human Subjects Research Protocols
UWZ-C-619	Safety Reporting for Clinical Trials



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UWZ-C-621	Deviation and Unanticipated Problem Reporting for Human Subjects Research Protocols
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11. Forms and Appendices:

Form or Appendix Number	Title
None	

12. Document Revision History:

Version Number	Brief Description of Changes	Effective Date
00	New	17 Nov 08
01	Updated procedures to current processes and reference the appropriate SOPs and added AHRPO reporting requirements.	5 May 11
02	Clarified the background information and Updated references to incorporate the new Command Policy 2011-67.	<i>SEP 28 2011</i>