SOP Title	**AMENDMENTS TO HUMAN SUBJECTS RESEARCH PROTOCOLS**	SOP No.	UWS-HP-615
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Signatures and Dates:

Authors:

QA Review:

Approving Authority:

Review/Approval for unchanged documents

	Author/Date	QA Review/Date	Approving Authority/Date
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1. Purpose and Applicability

This Standard Operating Procedure (SOP) describes the procedures for submitting, reviewing, and approving an amendment to research involving human subjects.

This SOP applies to the Walter Reed Army Institute of Research (WRAIR) Institutional Review Board (IRB), the WRAIR Principal Investigator (PI) or WRAIR Point of Contact (POC), the Human Subjects Protection Branch (HSPB), and the WRAIR Commander or Institutional Official (IO) acting on behalf of the WRAIR Commander.

2. Responsibilities

a. WRAIR HSPB staff members are responsible for:

1) Receiving the amendment, cover submission memorandum, and other supporting documentation.

2) Providing technical assistance and guidance to Principal Investigators (PIs) on the required format and documentation of an amendment covered under this SOP.

3) Providing a preliminary review of the submission to ensure federal regulations, DOD specific guidance, WRAIR Policy and ethical standards continue to be met.

4) Assuring the review of an amendment, and documenting the review.

5) Assuring that, if required, the amendment is forwarded to the WRAIR Scientific Review Committee (SRC) for scientific review and approval in accordance with WRAIR SOP UWS-002, Scientific Review of Human Use Protocols.

6) Officially transmitting the proposed amendment to the U.S. Army Medical Research and Development Command (USAMRDC) Office of Research Protections (ORP) Human Research Protection Office (HRPO) **IF** such approval is required for the amendment. Once the USAMRDC ORP HRPO approval is obtained, the WRAIR IO may provide authorization to implement.

b. The WRAIR IRB Chair (or designee) is responsible for:

1) Reviewing and approving, if appropriate, an amendment that qualifies for the expedited review procedure [21 CFR 56.110 (b), 32 CFR 219.110(b) and 45 CFR 46.110(b)], in accordance with this SOP.

2) Forwarding any amendment that increases risk to subjects or does not qualify for the expedited review procedure to the fully convened WRAIR IRB.

c. The WRAIR IRB is responsible for reviewing and recommending approval, if appropriate, of an amendment to approved research, in accordance with this SOP.

d. The WRAIR Commander/IO is responsible for authorizing an amendment for implementation or not authorizing the request in accordance with this SOP.

e. Investigator Guidance:

The PI or WRAIR POC (if PI is not at WRAIR) is expected to:

1) Submit electronic versions of the protocol amendment and all supporting documentation to the HSPB for review via email at usarmy.detrick.medcom-wrair.mbx.hspb@mail.mil. The submission should include:

a) a signed cover submission memorandum through the PI's Department/Branch and/or Director that describes and justifies the amendment and includes information about changes in the level of risk to human subjects; and

b) the revised protocol, signed protocol page, and any other applicable documents (e.g. informed consent forms, investigator's brochures, study staff documentation, etc.). Both a tracked change version and a clean

copy of the revised document(s) need(s) to be submitted with appropriate version control.

2) Reply to any comments made by the HSPB, the SRC, the IRB Chair (or designee) or the fully convened IRB in a timely manner (within 30 days after receipt of comments), until the amendment has been approved, disapproved, or withdrawn. Note: This may include revising the submitted documents and resubmitting with the new version numbers and dates. The response should not include “to be revised at the next amendment” language.

3) Assure that the amendment has received IRB and WRAIR Commander/IO approval prior implementation, except in cases where there are immediate hazards to human subjects.

4) Add the amendment IRB approvals and all documentation related to the amendment to the official regulatory file.

5) Report all amendments that occurred in the Continuing Review Report, as applicable.

6) Assure that when responding to stipulations of approval the response to these includes an amendment to address any changes to the protocol documents, as necessary, within 30 days of receipt of the stipulations. The response should not include “to be revised at the next amendment” language. For stipulations to the initial approval, an update to IRB approval may be submitted in lieu of an amendment.

3. Materials and Equipment

Not applicable

4. Procedures

a. HSPB Staff is expected to:

1) Document receipt of the amendment according to WRAIR SOP, Submission of Human Subjects Research Protocols and Consent Forms for Review, UWS-HP-623.

2) Review the amendment to ensure the submission packet is complete, per the Submission Checklist (refer to WRAIR SOP UWS-HP-623, Submission of Human Subjects Research Protocols and Consent Forms for Review), for consistency across documents, make preliminary assessment whether the

amendment continues to meet federal regulations, DOD guidance, and ethical standards, and confirm if it was reviewed by an approvable SRC.

3) Administrative changes, such as changes in telephone numbers and/or study personnel, do not require scientific review.

4) If necessary, submit the protocol to the SRC for review in accordance with the WRAIR SOP UWS-002, Scientific Review of Human Use Protocols.

5) Submits the amendment to the IRB Chair (or designee), if it is eligible for expedited review; or schedules it for review at a meeting of the fully convened IRB. Note: If an amendment requires full-convened IRB review, it will need to be reviewed by an IRB member prior to the meeting who can report on the amendment to the full IRB, in accordance with WRAIR SOP UWS-610, Institutional Review Board Meetings and Voting Requirements.

6) Notify the PI in writing of the following amendment review results:

   a) Approval - The IRB Chair or the convened IRB approves the amendment, and the Commander authorizes the amendment for implementation;

   b) Request for additional revision(s) - A written request from the IRB Chair or the convened IRB for additional changes/information to resolve issues prior to further action; and

   c) Disapproval - A written communication to the PI that includes the reason(s) for the disapproval.

7) Assure that the applicable authorizations (for example, a Food and Drug Administration exemption), agreements (for example, an IRB Authorization Agreement), and approvals (for example, local IRB approval or HRPO approval) are in place prior to Commander implementation approval.

8) For an amendment that requires review by the USAMRDC ORP HRPO prior to Commander implementation approval, submit a copy of the amendment and supporting documentation, as well as, WRAIR IRB approval, to USAMRDC ORP HRPO (usarmy.detrick.medcom-usamrmc.other.hrpo@mail.mil) for appropriate review and approval.

Note: For all amendments, approval is effective only until the expiration date of the most recent continuing review, as applicable.

9) Inform the IRB of amendments approved via the expedited review procedure by including a summary of the amendments approved in the IRB meeting materials at the next scheduled IRB meeting, in accordance with WRAIR SOP UWS-HP-616.

10) Maintain a copy of the amendment and documentation of the scientific and ethical review process in the protocol file. As appropriate, update the HSPB database with all milestones; ensure other information continues to be up to date.

11) Include in the IRB Commander approval letters a statement that no changes may be made to an approved protocol without prospective IRB re-review and approval.

12) Provide guidance on amendment requirements and post guidance on the HSPB website to PIs.

13) Ensure that the discussion of issues with respect to the amendment and the results of the voting during the fully convened IRB meeting are included in the IRB meeting minutes in accordance with WRAIR SOP UWS-HP-628, Review of Human Subjects Research by the Fully Convened WRAIR Institutional Review Board.

b. The Chair of the IRB (or designee) is expected to:

1) Review the amendment and determine if it qualifies for the expedited review procedure permitted by 21 CFR 56.110(b), 32 CFR 219.110(b) and 45 CFR 46.110(b), or requires review by the fully convened IRB (Refer to WRAIR SOP UWS-HP-613, Expedited Human Subjects Research Protocol Review). Examples of changes that may qualify for expedited review are: adding or removing an investigator, changes in advertising, or extension request. Examples of changes that require fully convened board are: a significant change in the study design, or the addition of a procedure that increases the risk to subjects beyond those defined as minimal risk. The IRB Chair or IRB Administrative Director has the authority to schedule any amendment for full-board review if, in their judgment, such review is necessary.

2) Under the expedited review procedure, take one or more of the following actions after amendment review:

a) Approval of the amendment.

b) Submit a written request to the PI, through HSPB staff, for additional changes/information to resolve issues prior to further action.

c) Submits an amendment that, in their judgment, should be reviewed by the fully convened IRB for review, instead of by expedited review to a convened IRB meeting for review.

3) Determine whether the amendment potentially affects study participants and/or their willingness to continue or enroll in the study. If the proposed amendment affects the participants' willingness to participate in the study, the IRB Chair (or designee) may request that the PI draft a contact plan and provide written materials with which to contact participants. A plan to re-consent subjects may be necessary.

4) Notify the PI in writing of the IRB's vote to disapprove and includes the reason(s) for the disapproval.

c. The WRAIR IRB is expected to:

1) Approve (with or without stipulations), table, or disapprove the amendment after review at a fully convened IRB meeting (Refer to WRAIR SOP UWS-610, Institutional Review Board Meetings and Voting Requirements).

2) Determine whether the amendment affects study volunteers and whether it might affect their willingness to continue or enroll in the study. If the proposed amendment may affect the volunteers' willingness to participate in the study, the WRAIR IRB may request that the PI draft a contact plan and provide written materials with which to contact participants. A plan to re-consent subjects may be necessary.

3) Review the drafted Communication to PI for completeness and accuracy (for primary and secondary reviewers only).

4) Review of the expedited list and corresponding approvals or review memorandums.

5. Explanation of Abbreviations, Acronyms, and Definition of Terms

Abbreviations and acronyms have been defined in the text at the time of first use.

Amendment	Any change in approved research which may include but is not limited to: adding or removing investigators, changing the consent form or method of advertising for the study, or modifying the study design.
Expedited Review	A procedure permitted by 21 CFR 56, 32 CFR 219 and 45 CFR 46, by which a protocol, amendment, continuing review/final report, or other report may be reviewed and approved for human subjects research activities without being reviewed at a fully convened meeting of an IRB. Under the expedited review procedure, the review may be carried out by the IRB Chairperson or by one or more reviewers designated by the Chairperson from among members of the IRB.
Full Board Review	For this SOP: review of proposed changes to research at a convened meeting at which a majority of the membership of the IRB is present including at least one member whose primary focus is in nonscientific areas. For the change to be approved, it must receive the approval of a majority of those members present at the meeting.
IO	Institutional Official. Individual ultimately responsible for implementation of the U.S. Department of Health and Human Services (DHHS) Federal Wide Assurance and DOD Assurance of Compliance for the Protection of Human Research Subjects and the associated Human Research Protection Program (HRPP) at an institution engaged in research involving human subjects. Within the USAMRDC, the Commander of the institution/organization engaged in research is the IO.
IRB	Institutional Review Board. A committee that has been formally designated to review, approve, and monitor biomedical and behavioral research involving humans with the aim to protect the rights and welfare of the research subjects. Selection for the board is in accordance with Federal guidelines outlined in 21 CFR 56.107, 32 CFR 219, and 45 CFR 46.

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.
Minimal Risk	The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves those than ordinarily encountered in daily life or during performance of routine physical or psychological examination or tests (DHHS and FDA definition) OHRP further interprets this to be relative to the daily life of a normal, healthy person.
Research	A systematic investigation, including research development, and testing and evaluation, designed to develop or contribute to generalizable knowledge.

6. References

Reference Numbers or Author	Document Title
21 Code of Federal Regulations (CFR) 56	Food and Drug Administration, Institutional Review Boards
32 Code of Federal Regulations (CFR) 219	Department of Defense, Protection of Human Subjects
45 Code of Federal Regulations (CFR) 46	Health and Human Services, Protection of Human Subjects
Bankert, E. A. and Amdur, R. J.	Institutional Review Board Management and Function
AR 70-25	Use of Volunteers as Subjects of Research, 25 January 1990
FDA Guidance	Food and Drug Administration, Guidance for IRBs, Clinical Investigators , and Sponsors, IRB Continuing Review after Clinical Investigation Approval, February 2012

WRAIR SOP UWS-002	Scientific Review of Human Use Protocols
WRAIR SOP UWS-HP-613	Expedited Review of Human Subjects Research Protocols
WRAIR SOP UWS-HP-610	Institutional Review Board Meetings and Voting Requirements
WRAIR SOP UWS-HP-623	Submission of Human Subjects Research Protocols and Consent Forms for Review
WRAIR SOP UWS-HP-628	Review of Human Subjects Research by the Fully Convened WRAIR Institutional Review Board
OHRP	Guidance on Written IRB Procedures, 15 January 2007, http://www.hhs.gov/ohrp/humansubjects/guidance/irbgd107.htm

7. **Document Revision History**

Version Number	Brief Description of Changes	Effective Date
.00	New Document	22 March 2007
.01	Updated name and titles, revised per new scientific review SOP, and updated policies and procedures	31 March 2009
.02	Biennial Review; Updated for consistency with current policies/procedures.	6 April 2011
.03	Updated names and titles; revised per new scientific review SOP; and updated for consistency with current regulations, policies and procedures.	