Signatures and Dates:

Author:	Signatures on file
QA Review:	
Approving Authority:	

Review/Approval for unchanged documents

	Author/Date	QA Review/Date	Approving Authority/Date
1			

1. Purpose and Applicability

This Standard Operating Procedure (SOP) outlines the process used to conduct continuing review approval of non-exempt human subject research protocols subject to the Common Rule pre-2018 requirements and Revised Common Rule (2018 requirements).

Note: All non-exempt human subjects research protocols that received initial Institutional Review Board (IRB) approval *before* 21 January 2019, will undergo continuing review of research by the WRAIR IRB at intervals appropriate to the degree of risk, but no less than once per year. Continuing review will continue until the WRAIR IRB determines the protocol meets the requirements under the new Common rule OR an official final closure report has been submitted in accordance with WRAIR Commander's IRB Policy #07 and accepted by the WRAIR IRB.

Protocols approved prior to 21 January 2019 and the implementation of the 2018 Common rule (i.e., operating in accordance with the Pre-2018 Common Rule), may be eligible to submit a progress report instead of a continuing review report in accordance with SOP UWS-HP-638. Investigators interested in operating their research study under the rule changes, should contact the Human Subjects Protection Branch (HPSB) Point of Contact (POC) to determine what, if any, changes need to be made to the protocol and/or informed consent documents to be in accordance with the new requirements. The required changes must be submitted as an amendment to the protocol and receive all applicable approvals prior to implementation. **Continuing review of research by the IRB is required if the protocol is subject to the U.S. Food and Drug Administration (FDA) regulations or the WRAIR IRB determines so, regardless if the protocol meets the eligibility criteria listed below.**

All non-exempt human subjects research protocols that received initial approval *on or after* 21 January 2019 will require continuing review of research by the fully convened WRAIR IRB at intervals appropriate to the degree of risk, but not less than once per year**.** Continuing review of research by the fully convened WRAIR IRB is not required in the following circumstances:

(a) Research eligible for expedited review in accordance with 45 CFR 46.110 (Refer to SOP UWS-HP-613, Expedited Review of Human Subjects Research);

(b) Research reviewed by the IRB in accordance with the limited IRB review described in §46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8);

(c) Research that has undergone IRB review but has not yet:

(1) Received WRAIR Commander Authorization; or

(2) Received WRAIR Commander Authorization but has not yet initiated (i.e., not yet begun screening or enrollment of study participants).

Note: Research meeting conditions in point (c)(1) or (c)(2) above are eligible to use the abbreviated Continuing Review Report (Appendix 2b).

(d) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

(1) Data analysis, including analysis of identifiable private information or identifiable biospecimens; or

(2) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

The fully convened IRB may require protocols eligible for Institutional Progress Reports to undergo Continuing Review either via the expedited review process or review by the fully convened IRB. This decision is made at the time of initial review or at the time of subsequent life cycle actions at the discretion of the WRAIR IRB or IRB Chair. This decision may be made as a result of reports of serious non-compliance at the site or by a particular study team/individual, deviations, and/or type of study or product being evaluated.

Institutional progress reports will be required for all human subjects research protocols not requiring annual review by the WRAIR IRB in accordance with WRAIR SOP UWS-HP-638, Progress Reports. Note: If the WRAIR IRB relies on another Institution's IRB for review and that IRB does not require an annual progress report be submitted (e.g. minimal risk research), the HSPB continuing review POC will contact the study's WRAIR POC each year at the anniversary of the WRAIR Commander's approval, to request an update on whether WRAIR is still engaged in that research activity. This update can be provided via email communication.

NOTE: Eligibility of expedited continuing review, limited review or progress reporting does not preclude investigators from required reporting of various incidents to the IRB, such as Unanticipated Problems Involving Risks to Subjects or Others (UPIRTSOs), other reportable events, or from seeking prospective approval from the IRB for amendments to the research. (Refer to WRAIR SOP Deviations and Unanticipated Problem Reporting, UWS-HP-621 and WRAIR SOP Amendments to Human Subjects Research Protocols, UWS-HP-615.) This SOP applies to the WRAIR Commander/Institutional Official (IO), WRAIR IRB Members, the WRAIR IRB Chair/Designee, the WRAIR IRB Administrative Director, the HSPB), Staff and Principal Investigators (PI)/WRAIR POC. Templates for the Continuing Review Report/Application (Appendix 2a) and abbreviated Continuing Review Report/Application Form (Appendix 2b) are available on the WRAIR HSPB website and WRAIR intranet.

2. Background

The sponsor/funding agent of the study, collaborating institutions with or without IRBs, additional Department of Defense (DoD) review requirements, study location, and the risk

level of the study all contribute to how the continuing review is processed by the WRAIR IRB. In some situations, the WRAIR IRB oversees the conduct of an entire study. However, there are instances where the WRAIR IRB may limit their oversight to WRAIR-affiliated staff engaged in research, or certain sites in a multi-site study.
All IRBs must approve the continuing review by their established expiration date. The WRAIR Commander and/or WRAIR IRB can halt study activities in the event of a lapse in IRB approval; these activities include, but are not limited to: subject recruitment, screening and enrollment, intervention, subject interaction or follow-up with enrolled subjects, collection of data or specimens of analysis of data or specimens previously collected as part of the research protocol, publication and presentation of results to date. Subject interactions or follow-up may occur only if it is necessary to eliminate apparent and immediate hazards to the subject or to ensure subject safety.

For research sponsored by the WRAIR or sponsored by another DoD agency relying on the WRAIR IRB to ensure compliance with DoD regulations, collaborative IRBs must approve the continuing review prior to issuance of the WRAIR IRB continuing review acceptance memorandum. PI's communication with IRBs and collaborators at other institutions is critical to ensure effective review.

For protocols approved prior to 21 January 2019, there are three types of continuing review processes conducted by the WRAIR IRB or HSPB: 1) Fully convened WRAIR IRB review 2) Expedited review by the WRAIR IRB Chair (or Designee) and 3) WRAIR IRB Administrative Director (or designee) acknowledgment of continuing reviews performed by other institutions' IRBs (when the WRAIR relies on another institution for the IRB review of the protocol).

Note: Changes to the protocol (e.g. collaborative arrangements, risks to subjects) may result in a different category of continuing review process necessary to fulfill the regulatory requirements.

Other protocol lifecycle actions, such as amendments, extension requests, or reclassification requests, may be submitted with, but not as part of the continuing review packet. The IRB reviews these protocol lifecycle actions, as separate items in accordance to SOP UWS-HP-615, Amendments to Human Subjects Research Protocols. Items submitted with, or at similar time as the continuing review report application will be processed separately, with different processing timelines.

It is the responsibility of the PI to ensure extension or reclassification requests are submitted with enough time to be processed prior to the expiration or protocol closeout date. If these actions do not receive all appropriate approvals prior to expiration or close out dates, all study related activities must go on hold.

3. Responsibilities

Those taking responsibility for the actions in this SOP are the WRAIR IRB Chair/Designee, the WRAIR IRB Members, the WRAIR IRB Administrative Director, HSPB Staff, and the PIs. These persons are responsible for understanding the processes outlined in this SOP.

a. PI/WRAIR POC (responsibilities):

1. Track all IRB approvals, to include those from the collaborating institutions, as applicable, to ensure that they are all submitted in a timely manner. If feasible, in collaborative Outside the Contiguous United States (OCONUS) research with two or more IRB reviews, it may be preferable to have all IRBs communicate and agree on a single anniversary date to simplify the review process for the investigator. HSPB can give guidance to assist in this scenario. Ideally, the same continuing review report is submitted to all reviewing IRBs. Of note, it is the responsibility of the PI to know all continuing review dates associated with a specific study and ensure continuing review reports are submitted in a timely fashion to avoid expiration of the study. Additionally, the PI is responsible for reporting to the HSPB/IRB any lapse(s) in approval.

2. Submit the required continuing review report (appendix 2a or 2b), and associated documents, to the HSPB via the electronic mailbox and the HSPB POC, allowing sufficient time for review and continuation determination prior to the established continuing review date. The PI responds to all requests for information/additional documents from the HSPB and/or WRAIR IRB, and complies with any determinations made by the WRAIR IRB regarding the continuing review.

3. Select a cutoff date for the continuing review reporting period to achieve this deadline. The next continuing review reporting period should start on the day following the cutoff for the previous continuing review period so as to ensure a continual review of protocol activities by the WRAIR IRB.

4. For those protocols requiring full board review, submit the complete continuing review report/application 60-90 days before the established continuing review date; and for those protocols that qualify for expedited review, submit the continuing review report/application 30-60 days before the established continuing review date. Consult HSPB to ensure appropriate submission timelines are met.

5. If IRB approval lapses, ensure no human subjects research, including enrollment of new subjects or data/specimen analysis, is conducted on the protocol until the IRB continuation is granted, except when necessary to eliminate apparent immediate hazards to the subject. If study activities continue in order to eliminate immediate and apparent risk to subjects, the

PI is responsible to submit a report of the event and the study activities performed during the lapse to the WRAIR HSPB within 5 business days of the actions taken.

If investigators do not comply with the continuing review reporting requirements or research is suspended due to a lapse in the approval, the study is considered to be in in non-compliance. (Refer to WRAIR SOP, Non-Compliance Procedures, UWS-HP-606)

b. WRAIR IRB Chair/Designee (responsibilities):

1. Review continuing review report using Appendix 3;
2. Communicate with HSPB continuing review report POC and study team/PI to obtain any outstanding information for the continuing review report;
3. Present the continuing review report at the fully convened IRB review and communicate any newly identified risks, deviations, withdrawals, and potential issues to other board members;
4. Provide input and corrections to the Communications to PI and Approvals; and,
5. Sign continuation approval documents and return to the HSPB continuing review POC.

c. WRAIR IRB Members (responsibilities):

1. Review continuing review report and supporting documents using Appendix 3 to identify new or ongoing risks or benefits of the current research;
2. Communicate with the HSPB continuing review POC regarding any questions or concerns regarding information in the continuing review report;
3. Provide input and comment to the Communication to PI; and,
4. Review eligible continuing review reports via expedited procedures if delegated by the WRAIR IRB Chair.

d. WRAIR IRB Administrative director or Designee (responsibilities):

1. Assign the HSPB POC for the annual review; and
2. Review Communications to PI and approval memos for quality and Federal regulations.

e. HSPB Staff (responsibilities):

1. Send 90 day notifications as a courtesy to the study team (appendix 1);
2. Review initial submission, check for completeness, contact study team/investigator for additional information or required documentation using Appendix 3;
3. Schedule the review of the continuing review report at the appropriate IRB meeting;
4. Attend the IRB meeting and facilitate communication between IRB reviewers and the study team;
5. Draft the Communication to PI (if applicable), and obtain input from the IRB reviewers, HSPB Director and WRAIR IRB Chair prior to providing the communication to the PI;
6. Draft approvals, facilitate the quality control process with the HSPB Director and IRB reviewers and obtain approval signature;
7. Provide approval documentation to the study team;
8. Forward the signed annual review approval and supporting documents to collaborators or institutions for additional review (e.g., institutions relying on WRAIR for IRB review and HRPO) or maintenance within their regulatory file;
9. Update the continuing review report statuses within the HSPB database with new approval dates and relevant information and communications; and,
10. File appropriate documentation and communications in the electronic and paper protocol files.

4. Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP) Guidance for protocols approved prior to 21 January 2019

a. Determining Continuing Review Dates:

The WRAIR IRB recognizes the DHHS OHRP timelines for continuing review and approval. When the WRAIR IRB reviews and approves the continuing review within 30 days of the WRAIR IRB expiration date, the WRAIR IRB may retain the previously established expiration date for the protocol. If the continuing review approval occurs prior to 30 days before the expiration date, a new continuing review date must be established.

b. Multisite Research:

Continuing review of a multicenter research project by the local IRB must occur at least annually as long as the institution remains engaged in human subjects research activities involving the project, per the terms of the IRB's Federal Wide Assurance (FWA). Once the institution is no longer engaged in human subjects research activities under the project, there is no regulatory requirement for continuing review by the local IRB, even if human subjects research activities are occurring at other institutions. A site closeout report will need to be submitted to and accepted by both, the local IRB and the WRAIR HSPB/IRB.

c. Expedited review of greater than minimal risk research:

A study initially reviewed and approved as greater than minimal risk may qualify for expedited review under 32 CFR 219 (b)(ii) category 8. Application of category 8 to greater than minimal risk research is determined by the status of the study at the time the continuing review is submitted. For example, if a continuing review report for a greater than minimal risk study reports no subjects have been enrolled and no additional risks have been identified OR subjects participated in study interventions during the reporting period, but at the time the report is submitted, all interventions/interactions are complete, OR the study is limited to data analysis, the continuing review may be reviewed via expedited procedures.

5. Materials and Equipment – N/A

6. Procedures for Conducting Continuing Review:

a. As a courtesy, HSPB sends out continuing review notifications approximately 90 days prior to the expiration date of a study. The notification is sent out via email to the PI/WRAIR POC; additional POCs may be included on the correspondence. (See Appendix 1). The PI is responsible for the timely submission of annual review documents regardless of receiving 90 Day notification.

b. The investigator prepares and submits the continuing review packet to the HSPB inbox using the corresponding WRAIR IRB forms (See Appendices 2a, 2b) or templates from other IRBs containing equivalent information (for protocols or collaborating sites).

Note: WRAIR IRB review is independent of local IRB review. The PI/WRAIR POC should prepare and submit the continuing review report regardless of the status of the reviews being performed by collaborating IRBs (if any). Local approvals must be obtained prior to issuing the WRAIR approval for the annual review.

c. The continuing review packet is subsequently forwarded to the HSPB continuing review POC, who reviews the submission using the HSPB and WRAIR IRB

Member Continuing Review Checklist (Appendix 3). The HSPB continuing review POC contacts the PI or WRAIR POC to address any deficiencies noted in the review packet. Responses and any remaining questions or deficiencies are included with the continuing review packet for review by the full IRB, IRB Chair, or IRB Chair designee.

d. The continuing review package is reviewed by either:

1. Expedited review processes in accordance with SOP UWS-HP-613; or

2. Full board review, in accordance SOP UWS-HP-628.

The WRAIR IRB makes a risk determination for activities in the upcoming continuing review period, determining whether the level of risk to subjects remains the same or has changed. The review results in one of the following:

1) The protocol and report are approved as written;
2) The protocol and report are approved with stipulations;
3) The protocol is suspended and all research related activities must go on hold; or,
4) The protocol is disapproved and terminated.

Notes: Reviewers should include HSPB in all email communications with the PI or WRAIR POC of the protocol, or communicate topics discussed during phone calls with the PI/WRAIR POC to HSPB staff to document and retain in the WRAIR IRB protocol file.

The WRAIR IRB approval period must also be documented, and may be no more than 12 months. If the protocol receives a review period of less than 12 months, a justification must be documented in the approval.

Study teams have 30 days to respond to stipulations unless otherwise specified by the WRAIR IRB, IRB Chair, or IRB Chair Designee in the Communication to PI or continuing review report approval.

e. For protocols where WRAIR relies on another institution for IRB review, the continuing review report or annual report is conducted by the Director, HSPB (or Designee) results in either:

1) Acknowledgement of the other institution's supporting continuing review documentation and IRB approval;

2) Recommendations to the IRB Chair/Human Protections Administrator of the other Institution; or

3) Recommendation to the WRAIR Commander/IO to dissolve the Institutional Agreement for IRB Review (IAIR) and require the submission of a full continuing review packet to the WRAIR IRB (Refer to SOP UWS-HP-624, Working with Other Institutions Engaged in Research [Assurances, IAIRs, and Reliance Agreements]).

f. Once a final continuation determination by the IRB, IRB Chair/Designee, or HSPB Director/Designee, has been made and documented, it is returned to the HSPB continuing review POC who:

1) For protocols reviewed by the fully convened IRB, the HSPB continuing review POC will send a communication to the PI following the meeting, summarizing the outcome of the review and stipulations (if any). Additionally, an official acceptance letter, signed by the WRAIR IRB Chair or Designee, will be sent to the PI/WRAIR POC. For those studies approved with stipulations, the review of the stipulations may be addressed under separate cover; and

2) For progress reports or external IRB reviews received by the HSPB Director/Designee, the POC will issue the email acknowledgement communication to the WRAIR POC.

Note: For actions approved by the full board as written, no additional communication to PI is required. The official acceptance letter is sufficient in this case.

g. Storage of records documenting the WRAIR IRB continuing review

The continuing review package, correspondence between the WRAIR IRB and the investigator, a copy of the progress report acknowledgement/ acceptance or suspension/termination communication to the PI and, as applicable, a copy of the WRAIR IRB meeting minutes relating to that protocol are filed in the HSPB regulatory files.

The PI is also required to maintain a regulatory file, continuing review and corresponding documentation for the timeframe specified per his/her institutional requirement.

h. The WRAIR continuing review POC updates the HSPB database with new expiration date and relevant information regarding the annual review.

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

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

8. References

Reference Number or Authors	Document Title
AR-70-25	Use of Volunteers as Subjects of Research, 25 January 1990
DoDI 3216.02	Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research, 15 April 2020
FDA Guidance	IRB Continuing Review after Clinical Investigation, February 2012 Approval
ICH-GCP-E6	*Guideline for Good Clinical Practice.*
Titles 21, 32 and 45	*Code of Federal Regulations*
63 Federal Register (FR) 60364-60367	National Institutes of Health. Protection of Human Subjects: Categories that May Be Reviewed by the Institutional Review Board through an Expedited Review Procedure, 9 November 1998
Amdur, R. J. and Bankert, E. A.	Institutional Review Board Management and Function. Boston: Jones and Bartlett Publishers, 2006, Second Edition
WRAIR Commander's IRB Policy Memorandum #03	Initial and Ongoing Human Subjects Protection Education and Training Requirements
WRAIR Commander's IRB Policy Memorandum #02	Determination that an Activity is Research Involving Human Subjects
WRAIR Commander's IRB Policy Memorandum #07	Human Subjects Research Protocol Closure Policy
WRAIR HSPB Document	Master List of Definitions, (Pending)
WRAIR SOP UWS-HP-606	Non-Compliance Procedures
WRAIR SOP UWS-HP-613	Expedited Review of Human Subjects Research

WRAIR SOP UWS-HP-615	Amendments to Human Subjects Research Protocols
WRAIR SOP UWS-HP-621	Deviations and Unanticipated Problem Reporting
WRAIR SOP UWS-HP-624	Working with Other Institutions Engaged in Research (Assurances, IAAs, & Reliance Agreements)
WRAIR SOP UWS-HP-634	Directed-Monitoring of Human Subjects Research
WRAIR SOP UWS-HP-638	Progress Reports and Continuation Determination

7. Appendices and Attachments

Appendix or Attachment Number	Title
UWS-HP-618-A-1	Continuing Review Notifications
UWS-HP-618-A-2a	Continuing Review Report Application
UWS-HP-618-A-2b	Abbreviated Continuing Review Report Application
UWS-HP-618-A-3	HSPB and WRAIR IRB Member Continuing Review Worksheet

8. Document Revision History

Version Number	Brief Description of Changes	Effective Date
.00	Original SOP	01 Feb 2008
.01	Re-Organization of SOP outline for readability, update SOP and appendices with current WRAIR policies and procedures	12 Aug 2009
.02	Revise SOP in accordance with existing OHRP guidance and DoD policies and procedures	15 Jan 2016

.03	Revise SOP in accordance with OHRP guidance on pre-2018 and Revised Common Rule (2018) requirements and DoD policies. Closeout processes removed and placed in a new SOP	04 Dec 2020