Standard Operating Procedure
Walter Reed Army Institute of Research

SOP:	**EXPANDED ACCESS TO INVESTIGATIONAL PRODUCTS FOR TREATMENT USE**	**SOP No.:**	UWS-HP-604
		Version:	.04
Effective Date:	21 June 2024	**Page:**	1 of 10

Signatures and Dates:

Author:

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) outlines the process for the submission, review, and approval of expanded access use protocols for investigational drugs, biologics, devices or combination products, (also referred to compassionate use) at, or involving, the Walter Reed Army Institute of Research (WRAIR). Expanded access use protocols of investigational new drugs (IND) and investigational device exemptions (IDE) allow access to the test article/device for patients who do not meet the criteria for inclusion in an existing approved clinical trial and who have a serious or immediately life-threatening disease or condition, and for whom the investigator and treating physician feels expanded access use presents a benefit in treating, mitigating and/or diagnosing their disease or condition. Prospective U.S. Food and Drug Administration (U.S. FDA), Sponsor and Institutional Review Board (IRB) approval are required prior to expanded access use. The requirement for a written submission may be initially waived by the U.S. FDA in emergency use situations. For emergency use situations, refer to WRAIR SOP UWS-HP-607: Emergency Use Notification and Reporting Procedures.

Recognizing that the WRAIR is not a medical treatment facility (MTF), but that WRAIR personnel may participate (i.e. as an investigator, treating physician, subject matter expert, supplier of the investigational product or other support) in expanded access use protocols, the WRAIR Institutional Official (IO) relies upon the IRB that has jurisdiction of the MTF or treatment center at which the protocol will be conducted for review of expanded access use protocols, when WRAIR personnel are engaged in human subjects research as defined in 32 CFR 219.102 and the IO supports WRAIR's participation in the activity.

2. Roles & Responsibilities

a. The HSPB Staff are responsible for:

1) Verifying that the submission for the expanded access use protocol is complete.
2) Ensuring that the appropriate Institutional Agreement for IRB Review (IAIR), as applicable, is in place between WRAIR and the Reviewing Institution.

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3) Ensuring that the WRAIR reporting/oversight language is included in the protocol, as appropriate.
4) Providing a recommendation to the HSPB Director, Deputy Director, or Designee on whether or not the expanded access use protocol is a human subjects research activity where WRAIR is engaged in human subjects research.
5) Preparing and sending communications/memoranda to the Principal Investigator (PI) and/or WRAIR point of contact (POC) regarding the protocol on behalf of the IO.
6) Preparing the regulatory binder(s) for the protocol, archiving all documentation corresponding to the protocol in the regulatory binder(s) and updating the HSPB database, as appropriate.

b. The HSPB Director, Deputy Director, or Designee, is responsible for review and determination as to whether or not the expanded access use protocol is a human subjects research activity where WRAIR is engaged in human subjects research.

c. The IO or Designee is responsible for:

1) Reliance on the appropriate institution for IRB review of the expanded access use protocols.
2) Final approval authority of expanded access use protocols on behalf of WRAIR.

d. The participating Branch/Directorate Director is responsible for notifying the WRAIR HSPB when the expanded access IND/IDE goes into effect and for reporting the results to the WRAIR HSPB in real time once the expanded access use protocol has been completed.

3. Investigator Guidance

WRAIR Investigators are advised to:

e. Comply with the U.S. FDA submission requirements outlined in 21 CFR 312.305, 310, 315, and 320, and 812.35(a), as appropriate, for expanded access use protocols. The investigator will need to consult with the Office of The

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Surgeon General (OTSG) Sponsor's Representative/U.S. Army Medical Research and Development Command (USAMRDC) Office of Regulated Activities (ORA) and/or Sponsor (for non-OTSG sponsored-studies) for guidance and assistance with the expanded access IND and IDE applications, as additional Sponsor requirements will apply. Note: U.S. Army personnel may not serve as an investigator-sponsor of a U.S. FDA-regulated protocol.

f. Comply with the U.S. FDA requirements as it relates to investigators to include ensuring compliance with the informed consent requirements set forth in 21 CFR 50, that the IRB review/approval requirements are satisfied as set forth in 21 CFR 56, maintaining accurate case histories, drug disposition records and retaining records in a manner consistent with the requirements of 21 CFR 312. 62 and 305 or 21 CFR 812.140, as applicable, and the reporting of adverse drug events or adverse device effects to the Sponsor, as per 21 CFR 312.305 or 21 CFR 812.140, as applicable.

g. Submit a protocol submission packet to the WRAIR HSPB, including overseeing reviewing IRB approval(s), as per WRAIR Commander's IRB Policy Memorandum #24, Submission Requirements for Human Subjects, their Information or Biospecimens.

h. Respond to requests for documentation and information from the WRAIR HSPB, USAMRDC ORA, and reviewing IRB(s).

i. Comply with the terms of the WRAIR administrative review, WRAIR IO approval, and approval from the reviewing IRB(s) and their IOs.

j. Notify the overseeing reviewing IRB(s) and WRAIR HSPB in the event that a clinical hold is imposed by the U.S. FDA for the expanded access use protocol.

k. Initiate the expanded access use protocol only when the expanded access IND or IDE goes into effect 30 days after the U.S. FDA receives the submission (or sooner if permitted by the U.S. FDA).

l. Notify the overseeing reviewing IRB(s) and WRAIR HSPB when the expanded access IND/IDE goes into effect. Also, responsible for reporting the results to

the WRAIR HSPB in real time once the expanded access use protocol has been completed.

m. Maintain correspondence with the U.S. FDA, USAMRDC ORA, WRAIR HSPB, WRAIR IO, and reviewing IRB(s) and IOs.

4. Procedures

a. HSPB staff verifies that the expanded access use protocol submission is complete. The expanded access use protocol submission should include the following:

1) Expanded Access Use protocol; the protocol must include the following information:

a) The rationale for the intended use of the drug, biologic, combination product, or device, including a list of available therapeutic options that would ordinarily be tried before resorting to the investigational drug, biologic, combination product, or device or an explanation of why the use of the investigational drug, biologic, combination product, device is preferable to the use of available therapeutic options;
b) The criteria for patient selection or, for an individual patient, a description of the patient's disease or condition, including recent medical history and previous treatments of the disease or condition;
c) The method of administration of the drug/biologic/combination product, dose, and duration of therapy or instructions for use for the device and all other labeling as required under 812.5(a) and (b);
d) Identification of any changes from the existing approved clinical protocol necessary to treat the patient(s);
e) A discussion of why the patient(s) does(do) not qualify for use of the test article/device under an existing approved protocol;
f) Pharmacology and toxicology information adequate to conclude that the drug/biologic/combination product is reasonably safe at the dose and duration proposed for expanded access use (ordinarily, information that would be adequate to permit clinical testing of the

drug/biologic/combination product in a population of the size expected to be treated);

g) A description of clinical procedures, laboratory tests, or other monitoring necessary to evaluate the effects of the drug, biologic, combination product, or device and minimize its risks; and

h) When patients will be charged for a drug, biologic, combination product, or device, being made available for expanded access the submission should specify what costs can be recovered by the drug manufacturer. (Note: When charging for an expanded access use the direct cost of the drug, biologic, combination product, or device, plus the costs of administering the expanded access program can be recovered).

2) A copy of the informed consent form to be used with the patient(s).

3) A submission letter signed through the Branch Director/Commander requesting WRAIR review.

4) A copy of the independent assessment by an uninvolved physician.

5) A copy of the letter of approval from the Sponsor/Sponsor's Representative/USAMRDC ORA.

6) A copy of correspondence from the U.S. FDA approving the expanded access use IND/IDE. Telephone logs from the Sponsor regarding U.S. FDA approval will be accepted as evidence of U.S. FDA approval if the IRB Administrative Director can verify approval with the U.S. FDA reviewer (by telephone or email).

7) A copy of any IRB approvals from the MTFs/MEDCENs and other collaborating institutions (if applicable), including copies of the minutes from the IRB meeting which detail that the conditions of 21 CFR 56 are met. In the case of individual patient expanded access INDs, the physician can request a waiver of the requirement for review and approval at a convened IRB meeting by completing Form FDA 3926, where the physician would obtain the IRB chair/designee concurrence prior to treatment use. In this case, a copy of the IRB chair/designee concurrence would be required in place of the meeting minutes from the IRB meeting.

8) Copies of the PI and WRAIR investigators' curricula vitae and Human Subjects Protection (HSP) training.

b. Expanded Access Use protocols are administratively reviewed by the WRAIR HSPB, to ensure WRAIR reporting/oversight requirements have been included as appropriate. The HSPB forwards pre-review comments to the overseeing IRB(s) as needed.

c. The Director, HSPB (or Designee) reviews the submission documents and makes a determination of engagement in research in accordance with WRAIR Commander IRB Memorandum #2, Determination that an Activity is Research Involving Human Subjects, as appropriate.

d. The WRAIR IO is the final approval authority for WRAIR personnel's participation in or support of expanded access use protocols; See SOP UWS-HP-624, Working with Other Institutions Engaged in Research [Assurances, IAAs, & Deferrals].

e. For use of a humanitarian use device, refer to a separate SOP, UWS-HP-605, Humanitarian Use Devices.

f. For emergency use, please refer to SOP UWS-HP-607, Emergency Use Notification and Reporting Procedures.

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

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

6. References

Reference Number or Author	Document Title
AR 40-7	Use of US Food and Drug Administration Regulated Investigational Products in Humans Including Schedule I Controlled Substances

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AR 40-68	Clinical Quality Management
WRAIR IRB Charter	Walter Reed Army Institute of Research (WRAIR) Charter
WRAIR HRPP	Walter Reed Army Institute of Research (WRAIR), Human Research Protection Program (HRPP)
ICH-GCP-E6	Guideline for Good Clinical Practice
Titles 21, 32 and 45	Code of Federal Regulations
U.S. FDA	Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers, Guidance for Industry, October 2017
U.S. FDA	Information on Expanded Access for Medical Devices (https://www.fda.gov/medical-devices/investigational-deviceexemption-ide/expanded-access-medicaldevices#compassionate)
U.S. FDA	Information on Expanded Access for Drugs (https://www.fda.gov/news-events/expandedaccess/expanded-access-categories-drugs-includingbiologics)
U.S. FDA	Individual Patient Expanded Access Applications: Form FDA 3926, Guidance for Industry, June 2016, Updated October 2017
WRAIR's Commander's IRB Policy #24	Submission Requirements for Human Subjects, their Information or Biospecimens
WRAIR Commander's IRB Policy Memorandum #25	Determination that an Activity is Research Involving Human Subjects
SOP UWS-HP-605	Humanitarian Use Devices

SOP UWS-HP-607	Emergency Use Notification and Reporting Procedures
SOP UWS-HP-624	Working with Other Institutions Engaged in Research [Assurances, IAAs, & Deferrals]

7. Appendices and Attachments

Reference Number or Author	Document Title
N/A	N/A

8. Document Revision History

Version Number	Brief Description of Changes	Effective Date
.00	New	18 Dec 2006
.01	Biennial review, including updates to organization names, references, procedural changes, and SOP name change for clarity.	16 Feb 2009
.02	Biennial review, including updates to references, procedural changes, and SOP name change for clarity.	06 April 2011
.03	Review and revisions to incorporate updated guidance, policies, and regulations	27 Jan 2021
.04	Reformatted using new WRAIR SOP template and other minor administrative and editorial changes, to include updates to references & procedural changes.	21 June 2024

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