

Walter Reed Army Institute of Research
 Division of Human Subjects Protection
 Standard Operating Procedure



SOP Title	EXPANDED ACCESS TO INVESTIGATIONAL DRUGS FOR TREATMENT USE	SOP No.	UWZ-C-604
Effective Date	APR 06 2011	Version	.02
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Signatures and Dates:

Author:

QA Review:

Approving Authority:

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

Review/Approval for unchanged documents

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

This Standard Operating Procedure (SOP) outlines the procedures for the submission, review, and approval of expanded access use protocols for investigational drugs, biologics or devices (also referred to as compassionate use) at the Walter Reed Army Institute of Research. Expanded access use protocols of investigational new drugs (IND) allow access to the test article 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 feels expanded access use represents a benefit in treating and /or diagnosing their disease or condition. Prospective Food and Drug Administration (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 FDA in emergency use situations.

Recognizing that the WRAIR is not a medical treatment facility (MTF), but that WRAIR investigators may participate in expanded access use protocols at the Department of Defense (DoD) medical centers (MEDCENS), the WRAIR Institutional Official (IO) defers review of expanded access use protocols to the DoD IRB that has jurisdiction of the MTF at which the protocol will be conducted.

2. Responsibilities

a. The DHSP Staff are responsible for

- 1) Ensuring that the submission for the expanded access use protocol is complete
- 2) Ensuring that the appropriate Institutional Agreement for IRB Review (IAIR) is in place between WRAIR and the DoD MTF IRB.
- 3) Ensuring that the WRAIR reporting/oversight language is included in the protocol, as appropriate.
- 4) Preparing and sending communications/memorandums to the Principal Investigator (PI) regarding the protocol on behalf of the IO.
- 5) Preparing the regulatory binder(s) for the protocol and archiving all documentation corresponding to the protocol in the regulatory binder(s).

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- b. The DHSP 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) Deferral of IRB review for expanded access use protocols to the appropriate DoD MTF IRB.
 - 2) Final approval authority of expanded access use protocols on behalf of WRAIR.

3. Investigator Guidance

WRAIR Investigators are advised to:

- a. Comply with the FDA submission requirements outlined in 21 CFR 312.305, 310, 315, and 320, as appropriate, for expanded access use protocols. The investigator will need to consult with the U.S. Army Medical Materiel Development Activity (USAMMDA) and/or Sponsor (for non-USAMMDA sponsored-studies) for guidance and assistance with the expanded access IND 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.
- b. Comply with the 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 the reporting of adverse drug events to the sponsor.
- c. Submit a protocol submission packet to the WRAIR DHSP, including overseeing DoD MTF IRB approval(s), as per SOP, UWZ-C-623 entitled "Submission of Protocols and Consent Forms for Review."
- d. Respond to requests for documentation and information from the WRAIR DHSP, USAMMDA, and reviewing DoD MTF IRB(s).

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- e. Comply with the terms of the WRAIR administrative review, WRAIR IO approval, and approval from the reviewing DoD MTF IRB(s) and their IOs.
- f. Notify the overseeing DoD MTF IRB(s) and WRAIR DHSP in the event that a clinical hold is imposed by the FDA for the expanded access use protocol.
- g. Initiate the expanded access use protocol only when the expanded access IND goes into effect 30 days after the FDA receives the submission (or sooner if permitted by the FDA).
- h. Maintain correspondence with the FDA, USAMMDA, WRAIR DHSP, WRAIR IO, and reviewing DoD MTF IRB(s) and IOs.

4. Materials and Equipment

Not Applicable.

5. Procedures

- a. DHSP staff ensures that the expanded access use protocol submission is complete. The expanded access use protocol submission should include the following:
 - 1) Expanded Access Use protocol that includes the following information:
 - a) The rationale for the intended use of the drug, including a list of available therapeutic options that would ordinarily be tried before resorting to the investigational drug or an explanation of why the use of the investigational drug 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, dose, and duration of therapy;
 - d) Identification of any changes from the existing approved clinical protocol necessary to treat the patient(s);
 - (1) A discussion of why the patient(s) does/do not qualify for use of the test article under an existing approved protocol;



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- (1) Pharmacology and toxicology information adequate to conclude that the drug 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 in a population of the size expected to be treated); and
 - (2) A description of clinical procedures, laboratory tests, or other monitoring necessary to evaluate the effects of the drug and minimize its risks.
- 2) A copy of the informed consent form to be used with the patient(s);
 - 3) A submission letter signed through the Division 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/USAMMDA;
 - 6) A copy of correspondence from FDA approving the expanded access use IND. Telephone logs from the Sponsor regarding FDA approval will be accepted as evidence of FDA approval if the IRB Administrative Director can verify approval with the FDA reviewer (by telephone or email);
 - 7) A copy of any IRB approvals from the MEDCEN 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.
 - 8) Copies of the WRAIR investigators' curriculum vitas and human subjects protection training.
- b. Expanded Access Use protocols are administratively reviewed by the WRAIR DHSP, referred to as a pre-review, to ensure WRAIR reporting/oversight requirements have been included as appropriate. The DHSP forwards pre-review comments to the overseeing DoD MTF IRB(s) as needed.
 - c. The Director, DHSP (or designee) reviews the submission documents and makes a determination of engagement in research in accordance with WRAIR Policy Letter #08-03, Determination that an Activity is Research Involving Human Subjects, as appropriate.

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- d. The WRAIR IO grants implementation approval of the expanded access use protocol if all conditions of 21 CFR 56 are met as described in the IAIR between the WRAIR and the DoD MTF overseeing the protocol (See SOP UWZ-C-624, Working with Other Institutions Engaged in Research [Assurances, IAAs, & Deferrals]).
- e. For use of a humanitarian use device, refer to a separate SOP, UWZ-C-605, Humanitarian Use Devices.
- f. For emergency use, please refer to SOP UWZ-C-607, Emergency Use and Notification Reporting Procedures.

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6. Explanation of Abbreviations and Terms

Division of Human Subjects Protection (DHSP)	Division of Human Subjects Protection, WRAIR, is the administrative branch of the IRB.
DoD	Department of Defense
Expanded Access Use IND	Expanded Access Use Investigational New Drug (IND) is a mechanism for providing eligible subjects with investigational drugs for the treatment of a serious or immediately, life-threatening disease or condition and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition. An expanded access use IND may be granted after sufficient data have been collected to show that the drug "may be effective" and does not have unreasonable risks. Because data related to safety and side effects are collected, expanded access use INDs also serve to expand the body of knowledge about the drug.
FDA	Food and Drug Administration
Human Subjects Research	Research involving humans as research subjects, or involving human data and/or biological specimens, specimens from repositories or anatomical substances of human origin. This includes the administration of questionnaires or surveys, as well as research done in an educational setting.
IAIR	Institutional Agreement for IRB Review
Immediately, Life-Threatening Disease or Condition	A stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.
IND	Investigational New Drug
IO	Institutional Official

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- IRB Institutional Review Board
- MEDCENS Department of Defense (DoD) medical centers
- MTF Military Treatment Facility
- Research Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.
- Risk The probability of harm or injury (physical, psychological, social or economic) occurring as a result of participation in a research study.
- Serious Disease/Condition A disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one.
- SOP Standard Operating Procedure
- Test Article Any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act.
- WRAIR IRB WRAIR Institutional Review Board , the ethical review committee for research involving human subjects at WRAIR, its continental U.S. detachments or Overseas Laboratories, or when WRAIR funding, facilities or personnel are involved in any way (investigator, medical monitor, consultant, collaborator, etc.). This includes protocols for which recruitment of subjects is through WRAIR.

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USAMMDA US Army Medical Materiel Development Activity

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7. References:

Reference Number or Authors	Document Title
AR 40-7	<i>Use of U.S. Food and Drug Administration Regulated Investigational Products in Humans Including Schedule I Controlled Substances</i>
AR 40-68	<i>Clinical Quality Management, 26 February 2004</i>
AR 70-25	<i>Use of Volunteers as Subjects of Research, 25 January 1990</i>
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	<i>Guideline for Good Clinical Practice</i>
Titles 21, 32 and 45	<i>Code of Federal Regulations</i>
U.S. FDA	<i>Guidance for Institutional Review Boards and Clinical Investigators 1998 Update</i>
WRAIR Policy Letter #08-03	Determination that an Activity is Research Involving Human Subjects
SOP UWZ-C-605	Humanitarian Use Devices
SOP UWZ-C-607	Emergency Use Notification and Reporting Procedures
SOP UWZ-C-623	Submission of Protocol Documents and Consent Forms for Review
SOP UWZ-C-624	Working with Other Institutions Engaged in Research [Assurances, IAAs, & Deferrals]



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7. Forms and Appendices:

Form or Appendix Number	None
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9. Document Revision History:

Version Number	Brief Description of Changes	Effective Date
.00	New	18 Dec 06
.01	Biennial review, including updates to organization names, references, procedural changes, and SOP name change for clarity.	16 Feb 09
.02	Biennial review, including updated to references, procedural changes, and SOP name change for clarity.	APR 06 2011