

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



SOP Title	<b>HUMANITARIAN USE DEVICES</b>	SOP No.	<b>UWZ-C-605</b>
Effective Date	<b>APR 08 2011</b>	Version.	<b>.01</b>
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**Signatures and Dates:**

Author:

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

Approving  
Authority:

**Review/Approval for unchanged documents**

Date	Author	QA Review	Approving Authority

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- 1. Purpose/Applicability:** This Standard Operating Procedure (SOP) documents the process used by the Walter Reed Army Institute of Research (WRAIR) Institutional Review Board (IRB) to review submissions regarding a Humanitarian Use Device (HUD). WRAIR IRB review and approval is required for this use.

A HUD is one that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States in a calendar year. The purpose of a Humanitarian Device Exemption (HDE) is the protection of the public health and safety and within ethical standards, to encourage the discovery and use of devices intended to benefit patients in the treatment or diagnosis of diseases or conditions that affect fewer than 4,000 individuals in the United States. According to Section 520(m) of the Medical Device Amendments of 1976, the Food and Drug Administration (FDA) may exempt a HUD from the effectiveness requirements of sections 514 and 515 of the act provided that the device will be used to treat or diagnose a disease or condition affecting fewer than 4,000 individuals in the United States; the device would not be available unless the exemption were granted; there is no comparable device available; and the device will not expose patients to an unreasonable or significant risk and the probable benefit to health outweighs the risks from use.

A HDE is valid for 18-month intervals as long as certain criteria are met. A HUD cannot be sold for an amount that exceeds the costs of research and development, fabrication and distribution. Such devices may only be used in institutions where a local IRB has approved the use of the device to treat or diagnose the specific rare disease; absent IRB approval, the device cannot be used in humans. IRB approval is needed to ensure that provisions are in place so that the subject understands that the safety and efficacy of the device is unknown at present.

- 2. Responsibilities:** Those taking responsibility for the actions in this SOP are the WRAIR IRB members, the WRAIR IRB Administrative Director, Division of Human Subjects Protection (DHSP) Staff, and the WRAIR Institutional Official (IO).
  - a. The WRAIR IRB members:
    - 1) Review this SOP, and
    - 2) Review the HUD request according to the procedures outlined in this SOP and FDA guidance, and
    - 3) Review the appropriate pediatric information submitted by investigators and sponsors as part of the submission of a HUD, if applicable, and



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- 4) Issue approval or disapproval results to the investigator(s).
- b. The WRAIR DHSP Administrative Director and DHSP staff:
  - 1) Review and understand this SOP, and
  - 2) Review the appropriate pediatric information submitted by investigators and sponsors as part of the submission of a HUD, if applicable, and
  - 3) Ensure that the protocol materials are complete for submission to the WRAIR IRB for review.
- c. The WRAIR IO:
  - 1) Review this SOP, and
  - 2) Grant final approval for the HUD, if appropriate.

### 3. Investigator Guidance:

The Principal Investigator (PI) is expected to:

- a. Submit a protocol submission packet to the WRAIR IRB via the WRAIR DHSP.
- b. Respond to requests for documentation and information from the WRAIR IRB and WRAIR DHSP.
- c. Comply with the terms of approval from the IRB and IO.
- d. Consult with the U.S. Army Medical Materiel Development Activity (USAMMDA) when the HDE holder is the Office of The Surgeon General (OTSG) or when the HDE applicant is Army personnel.
- e. Maintain correspondence with the FDA and reviewing IRBs.

### 4. Materials and Equipment: Not Applicable.

### 5. Procedures:

- a. Review and approval recommendation by a fully convened WRAIR IRB is required before use of a HUD, as is WRAIR IO approval prior to implementation.
- b. Investigators and Sponsors submit the following documents to the IRB for review when submitting paperwork for a HUD:

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- 1) Protocol submission packet (Refer to WRAIR SOP UWZ-C-623, Submission Requirements).
- 2) FDA HDE Letter allowing use of the HUD.
- 3) Summary of Safety and Probable Benefits (from Sponsor).
- 4) Labeling for the device.
- 5) Adverse event reporting requirements and device defect reporting requirements, including updated information on a periodic basis demonstrating that the HUD designation is still valid, based on the most current and authoritative information available (21 CFR 814.126(b)). As part of these reporting requirements, the number of devices shipped or sold since initial HDE marketing approval must be reported (21 CFR 814.126(b)(1)(iii)).
- 6) To help FDA track information required for annual reporting to congress, premarket approval of medical devices should include requirements relating to the submission of information on pediatric subpopulations that suffer from the disease or condition that a device is intended to treat, diagnose, or cure, as required by the act, section 515A(a), Premarket Approval; General Requirements. FDA has concluded that the term 'pediatric patient' refers to patients who are 21 years of age or younger at the time of the diagnosis or treatment. Any request to the FDA for a humanitarian device exemption (HDE) should include information on the pediatric subpopulation. For a list of the specific information required, see the related sections in 21 CFR 814. These changes are effective August 16, 2010 and failure to submit the appropriate pediatric information can slow, or even stop, an FDA review.
- 7) FDA Annual Reports of HUD and continuing review reports.
- 8) Number of devices shipped or sold. If the number exceeds 4,000, an explanation and estimate of the number of devices used on multiple patients with a basis for the estimate.
- 9) Information describing the applicant's clinical experience with the device, any training completed or required, and a list of physicians who will be using the device.

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- 7) A statement from the investigator concerning whether or not state law and / or institutional policy requires informed consent.
- 8) Any agreements [Memorandum of Agreement (MOA), Memorandum of Understanding (MOU), Cooperative Research and Development Agreements (CRADA), IRB Authorization Agreements (IAA), Funding specifications, etc.].
- 9) Additional IRB approvals from collaborating sites.
- 10) Patient Information Sheet (prepared by the Investigator or Sponsor), which is also referred to as "patient labeling," that meets the following requirements:
  - a) Lay language (8th grade readability scale) used to inform the patient about the intended uses of the device (including that it is a HUD), relevant warnings, precautions, side effects and contraindications, and a statement that the effectiveness of the device has not been demonstrated;
  - b) Who to contact for questions about the device (Investigator's contact information);
- 11) Any advertisements or other descriptive materials used by the HDE holder or private label distributor;

Note: The Sponsor is responsible for post approval reporting requirements under 21 CFR 814.84 and 814.126.

- c. The WRAIR IRB will review the submission and determine if informed consent is required. The WRAIR IRB may also require that the subject sign and date the Patient Information Sheet prior to the HUD use.
- d. At the time of initial review, the WRAIR IRB will determine if approval of the use has any further restrictions on a case-by-case basis (such as: use of the device will be under a protocol). IRB approval may not exceed the scope of the FDA approved indication.
- e. At the time of initial review, the IRB will determine if continuing review may be expedited (per 21 CFR 56.110) for an approved device or if full board review is required.

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- f. Investigators submit a continuing review report to the WRAIR IRB at a time frame determined by the IRB, but at least annually. This report will include information describing the applicant's clinical experience(s) with the device.
- g. Investigators submit the following to the WRAIR IRB:
  - 1) Any amendments or supplements to the HDE.
  - 2) FDA Annual Reports from the Sponsor.
  - 3) Safety reports and Unexpected/Unanticipated adverse events or unanticipated problems.
  - 4) Increases in the incidence of anticipated adverse events.
  - 5) Reports of device failures necessitating a labeling, manufacturing or device modification.
  - 6) Any further results of animal / laboratory or clinical testing, when appropriate.
  - 7) Notification from the FDA regarding the suspension or withdrawal of the HDE.
  - 8) Any withdrawal of approval by a reviewing IRB.
  - 9) Final report from Sponsor.
  - 10) Final report from investigator.
- h. If the HUD is used in an emergency situation ("off label") to save the life or protect the physical well-being of a patient, conditions defined in the Code of Federal Regulations (CFR) must be met for emergency use. (Refer to WRAIR SOP UWZ-C-607, Emergency Use Notification and Reporting Procedures).
- i. If the HUD is used for compassionate use, refer to WRAIR SOP UWZ-C-604, Compassionate Use.

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**6. Explanation of Abbreviations and Terms:**

CFR	Code of Federal Regulations
CRADA	Cooperative Research And Development Agreement
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.
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.
Division of Human Subjects Protection (DHSP)	Division of Human Subjects Protection, WRAIR, is the administrative branch of the WRAIR IRB.
HDE	Humanitarian Device Exemption
HUD	Humanitarian Use Device
IAA	Institutional Authorization Agreement
IO	Institutional Official
MOA	Memorandum of Agreement
MOU	Memorandum of Understanding
OTSG	Office of the Surgeon General
PI	Principal Investigator or WRAIR POC



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**7. References:**

Reference Number or Authors	Document Title
AR-40-68	<i>Clinical Quality Management</i> , 26 February 2004.
AR-70-25	<i>Use of Volunteers as Subjects of Research</i> , 25 January 1990
AR-40-7	<i>Use of Food and Drug Administration- Regulated Investigational Products in Humans Including Schedule I Controlled Substances</i> , 4 January 1991
WRAIR IRB Charter	Walter Reed Army Institute of Research (WRAIR) Institutional Review Board (IRB) Charter
WRAIR HRPP	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 Industry and FDA Staff, Humanitarian Device Exemption (HDE) Regulation: Questions and Answers</i> , 19 June 2008
SOP UWZ-C-623	Submission of Protocol Documents and Consent Forms for Review
SOP UWZ-C-607	Emergency Use Notification and Reporting Procedures
SOP UWZ-C-604	Compassionate Use

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**8. 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 organization name updates, updates to procedures and references, and minor editorial clarifications	<del>APR 0 8 2011</del>