Standard Operating Procedure
Walter Reed Army Institute of Research

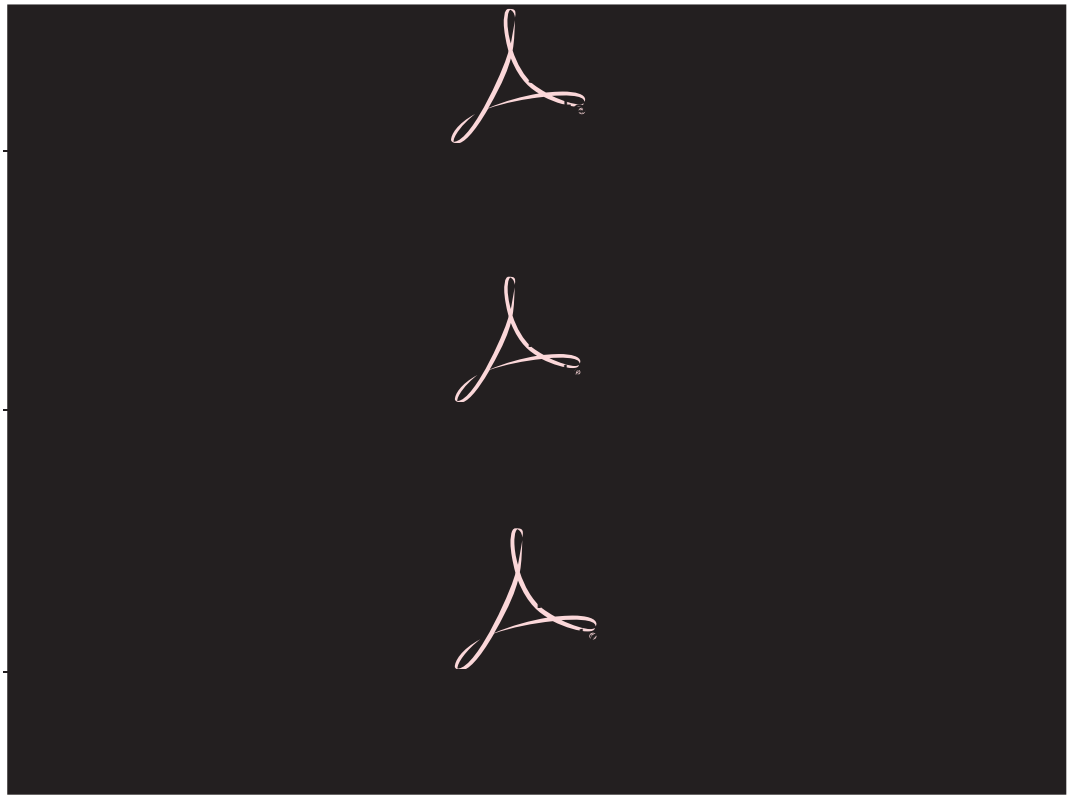
SOP:	HUMANITARIAN USE DEVICES	**SOP No.:**	UWS-HP-605
		Version:	.04
Effective Date:	21 June 2024	**Page:**	1 of 9

Signatures and Dates:

Author:

QA Review:

Approving Authority:



Review/Approval for unchanged documents

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1. Purpose and 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). HUDs are medical devices intended to benefit patients in the treatment or diagnosis of diseases or conditions that affect or are manifested in not more than 8,000 individuals in the United States per year.

Because the research has shown a HUD to have only "probable benefit," rather than "a reasonable assurance of effectiveness," every HUD requires IRB approval and oversight, whether for use in clinical care or in research. As the WRAIR is not a military treatment facility (MTF), WRAIR will rely upon the IRB that has jurisdiction where the device will be used (e.g., Department of Defense [DOD] medical centers) for IRB review.

As required by 21 CFR 814.104(b)(2), the applicant must provide a statement that no other comparable device, other than another HUD approved under an HDE or a device under an approved IDE, is available to treat or diagnose the disease or condition.

2. Roles & Responsibilities

a. The WRAIR IRB members/WRAIR IRB Chair (or Designee) are responsible for:

   1) Reviewing the initial and continuing review of the HUD request according to the procedures outlined in this SOP and U.S. Food and Drug Administration (US FDA) guidance.

   2) Reviewing the appropriate pediatric information submitted by investigators and sponsors as part of the submission of a HUD, if applicable.

   3) Issuing approval or disapproval decisions to the investigator(s).

b. The WRAIR Human Subjects Protection Branch (HSPB) Director and HSPB staff are responsible for:

   1) Verifying the HUD request is complete.

   2) Reviewing the appropriate pediatric information submitted by investigators and Sponsor(s) as part of the submission of a HUD, if applicable.

3) Ensuring that the protocol materials are complete for submission to the WRAIR IRB for review.

c. The Institutional Official (IO) or Designee is responsible for reviewing the HUD request and issuing final authority to execute it, if appropriate.

3. Materials and Equipment

Not Applicable.

4. Investigator Guidance

The Principal Investigator (PI) is expected to:

1) Upon Submit a protocol submission packet to the WRAIR IRB via the WRAIR HSPB (Refer to WRAIR SOP UWS-HP-623, Submission Requirements).

2) Respond to requests for documentation and information from the WRAIR IRB and WRAIR HSPB.

3) Comply with the terms of approval from the IRB and IO.

4) Consult with the U.S. Army Medical Research and Development Command (USAMRDC), Office of Regulated Activities (ORA), when the Humanitarian Device Exemption (HDE) holder is the Office of The Surgeon General (OTSG) or when the HDE applicant is Army personnel.

5) Maintain correspondence with the US FDA and reviewing IRBs decision(s).

5. Procedures

a. Review and approval by a fully convened IRB is required before use of a HUD, as is WRAIR IO approval authorization prior to implementation. USAMRDC component-level administrative review may also be required for use of HUD in certain populations, per USAMRDC Policy Memorandum 21.

b. Investigators and Sponsors must provide the following documents to the IRB for review when submitting a HUD request:

1) Protocol submission packet (Refer to WRAIR SOP UWS-HP-623, Submission Requirements).

2) U.S. 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, to include providing updated information on a periodic basis demonstrating that the HUD designation is still valid, based on the most current and authoritative information available [21 Code of Federal Regulations (CFR) 814.126(b)]. As part of these reporting requirements, the number of devices shipped or sold since initial HDE marketing approval must also be reported [21 CFR 814.126(b)(1)(iii)].

6) To help the U.S. 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. The U.S. FDA has concluded that the term 'pediatric patient' refers to patients who are younger than 22 years of age at the time of the diagnosis or treatment. Any request to the U.S. 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. Failure to submit the appropriate pediatric information can slow, or even stop, an U.S. FDA review.

7) U.S. FDA Annual Reports of HUD and continuing review reports.

8) Number of devices shipped or sold. If the number exceeds 8,000, 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.

10) A statement from the investigator concerning whether or not state law and / or institutional policy requires informed consent.

11) Any agreements [Memorandum of Agreement (MOA), Memorandum of Understanding (MOU), Cooperative Research and Development Agreements (CRADA), IRB Authorization Agreements (IAA), Funding specifications, etc.].

12) Additional IRB approvals from collaborating sites.

13) 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 and that no comparable device is available to treat the disease or condition), a description of any ancillary procedures associated with the use of the 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).

14) 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 following the review criteria in 21 CFR 56.111 and elsewhere in part 56, where applicable, 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 U.S. FDA approved indication.

e. At the time of initial review, the fully convened 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.

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 must submit the following to the WRAIR IRB:

1) Any amendments or supplements to the HDE.

2) U.S. FDA Annual Reports from the Sponsor.

3) Medical device reports (MDRs), safety reports and unexpected/unanticipated adverse events or unanticipated problems.

4) Increases in the incidence of anticipated adverse events.

5) Information reasonably suggesting that a HUD may have caused or contributed to a death or serious injury; or has malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

6) Reports of device failures necessitating a labeling, manufacturing, or device modification.

7) Any further results of animal / laboratory or clinical testing, when appropriate.

8) Notification from the U.S. FDA regarding the suspension or withdrawal of the HDE.

9) Any withdrawal of approval by a reviewing IRB.

10) Final report from Sponsor.

11) 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 CFR must be met for emergency use. (Refer to WRAIR SOP UWS-HP-607, Emergency Use Notification and Reporting Procedures).

i. If the HUD is used for expanded access, refer to WRAIR SOP UWS-HP-604, Expanded Access to Investigational Products for Treatment Use.

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

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

7. References

Reference Number or Author	Document Title
AR-40-68	Clinical Quality Management
AR-40-7	Use of Food and Drug Administration- Regulated Investigational Products in Humans Including Schedule I Controlled Substances
WRAIR IRB Charter	Walter Reed Army Institute of Research (WRAIR) Institutional Review Board (IRB) Charter
WRAIR HRPP	WRAIR Human Research Protection Program (HRPP)

ICH E6(R2)	Guideline for Good Clinical Practice
USAMRDC Policy	Command Policy 21
Titles 21, 32 and 45	Code of Federal Regulations
U.S. FDA	Humanitarian Device Exemption (HDE) Program, Guidance for Industry and FDA Staff, 06 September 2019
U.S. FDA	Guidance for Industry and FDA Staff, Humanitarian Use Device (HUD) Designations, Revision 1, 5 September 2019
SOP UWS-HP-623	Submission of Protocol Documents and Consent Forms for Review
SOP UWS-HP-607	Emergency Use Notification and Reporting Procedures
SOP UWS-HP-604	Expanded Access to Investigational Products for Treatment Use

8. Appendices and Attachments

Appendix or Attachment Number	Title
	None

9. Document Revision History

Version Number	Brief Description of Changes	Effective Date
.00	New	18 Dec 2006

.01	Biennial review, including organization name updates, updates to procedures and references, and minor editorial clarifications.	08 April 2011
.02	Review and revisions to incorporate updated guidance, policies, regulations, and minor editorial clarifications	30 Jan 2020
.03	Review and revisions to incorporate updated guidance, policies, regulations, and minor editorial clarifications	28 Feb 2024
.04	Reformatted using new WRAIR SOP template and other minor administrative and editorial changes.	21 June 2024