1. PURPOSE

This procedure describes the requirements for the review and documentation of the clinical use of a Humanitarian Use Device (HUD). If the intention of the Principal Investigator (PI) is to establish the safety and effectiveness of the HUD, however, the IRB will treat the study as an investigational drug or device study.

2. PROCEDURE

As defined in 21 CFR 814.3(n), and updated by the 21st Century Cures Act, a **Humanitarian Use Device** is a medical device that is intended to benefit patients in the treatment or diagnoses of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year and for which no comparable device is available. HUDs may only be used in institutions where a local IRB has approved the use of the HUD to treat or diagnose the specific rare disease. IRB approval is needed to ensure that there are provisions in place that allow for the human research subject to understand that the safety and efficacy of the HUD is unknown at present. A HUD is the only situation where federal regulations require the IRB to approve and monitor an activity that is clearly not research. Research is not required for the use of a HUD, and each IRB is free to establish its own criteria for IRB approval.

To be considered for HUD status, a device sponsor must complete a Humanitarian Device Exemption (HDE) application with the FDA. An approved HDE application authorizes the applicant to market the HUD. The labeling for the HUD must state that the device is a HUD and that the effectiveness of the device has not been demonstrated. The FDA approves HUDs based on evidence that it does not pose a significant risk of injury and that the potential benefit of the device to the health of the patient outweighs the risk of its use.

3. SPECIFIC PROCEDURES

3.1 Required Training

The PI and designated study team working with the HUD need to complete the required CITI training at least every three years:

- HUD Module, effective 7/7/2020.
- Prior completed modules within CITI are acceptable for training prior to 7/7/2020.

The PI will need to also read, sign and return to the IRB the following form: "Humanitarian Use Device (HUD) Lead Clinician Roles and Responsibilities – Acknowledgment Form."

3.2 Initial Review/PI Responsibilities

The PI or designee must submit to the IRB the following:

- FDA HDE Approval Letter which contains the following:
  - The generic and trade name of the device
  - The FDA HDE number
  - The date of HUD designation
- Manufacturer's Instructions for Use of the device / Package Label
- The HUD brochure / IRB Information brochure
- Patient information brochure or packet
- A written statement from the physician specifying:

- How the HUD will be used
- Who will be administering/implanting the HUD
- What are the clinical indications
- That the HUD will be limited to the clinical indications(s) listed in the FDA-approved product labeling
- That the HUD is not being used as a part of a research project or investigation designed to collect data to support an FDA pre-market approval application

- Note: Informed Consent is not required, but is at the discretion of the IRB and institution. The IRB may require the use of an informed consent, or may determine that the product labeling developed by the HDE holder incorporates enough information to assist a patient in making an informed decision about the use of the device.

3.3 Initial Review by the IRB

The HUD must be prospectively reviewed by a full IRB prior to use.

The Primary and Secondary Reviewers will verify that the provided documents for use of the HUD are congruent with the manufacturing labeling and the approved use under the HDE. The labeling for a HUD must state that the device is a Humanitarian Use Device and that, although the device is authorized by Federal Law, the effectiveness of the HUD for the specific indication has not been demonstrated.

The IRB has the discretion to determine the conditions of HUD use. For example, the IRB may approve the use of the HUD in general, or it may approve the HUD in a specific number of patients at this site, or they may approve it only under specific circumstances, etc. Although the FDA regulations do not require informed consent to use a HUD outside the setting of a research protocol, the IRB may require the use of an informed consent or may determine that the product labeling developed by the HDE holder incorporates enough information to assist a patient in making an informed decision about the use of the HUD.

No approval given by the IRB may exceed the scope of the FDA-approved indication of the HUD. Approval of a HUD will be granted for no more than one year.

3.4 Amendments

Amendments submitted for each individual use of the HUD may be reviewed at the expedited level.

Review of amendments, serious adverse events, or unanticipated problems to participants or others will be reviewed at the level for which criteria is met.

3.5 Continuing IRB Approval

Continuing review of the HUD may be reviewed at the expedited level. Approval of a HUD will be granted for no more than one year. Physicians requesting continuation must submit the following:

- Summary of all pertinent correspondence received from the holder of the HDE;
- A copy of the FDA-approved product labeling for the HUD, if it is different than what the IRB has already received; and

- A summary report of each patient in whom the HUD has been used during the previous six (6) months. Please include for each patient summary:
  - The clinical indications for the use of the HUD;
  - Any adverse events associated, or felt to be associated with the HUD; and
  - The clinical outcome of the HUD.

3.6 Permanent Closure

It is the responsibility of the PI to notify the IRB of closure of the HUD. This must include any notice from the manufacturer and the number of HUDs used. A manufacturer may receive Pre-Market Approval (PMA) and the HUD no longer qualifies for the HDE.

3.7 Prompt Medical Device Reporting

It is the responsibility of the PI to promptly report when he/she becomes aware of information, from any source, that reasonably suggests that a HUD has or may have caused or contributed to the death or serious injury of a patient. The PI will report to the FDA, as well as the IRB, within ten (10) business days of becoming aware of the information.

3.71 Prompt Reporting of FDA Actions on the HUD

It is the responsibility of the PI to promptly report to the IRB any FDA actions taken regarding the HUD for which the PI has become aware. The report will need to be sent to the IRB within ten (10) business days of the discovery.

Depending on the action, the IRB Chair or designee may need to take immediate action or await action until the full IRB has discussed the FDA action. If the IRB Chair or designee takes immediate action, it will be discussed and documented at the next full IRB meeting.

3.8 Use of a HUD outside of FDA approved indications

If a clinician decides to use a HUD outside of its approved indication(s) because there is no alternative device for a patient's condition, but is not yet to the level of an Emergency Use, the FDA strongly recommends that the treating clinician obtain the patient's informed consent. The FDA further recommends that the clinician establish reasonable patient protection measures, (for example, devising a schedule to monitor the patient) and submitting a follow-up report on the outcome and patient's condition to the HDE holder.

In addition to the above FDA recommendations, the Avera IRB expects that any time a HUD is used outside of its approved indication, that a detailed letter be submitted to the IRB explaining why it was used outside the FDA approved indications, if other physicians were consulted on this decision, when the HDE holder (i.e. Sponsor) and FDA were notified of its use, the response from the HDE holder and/or FDA, and the current status of the patient's condition after the HUD was used.

3.9 Emergency Use of a HUD

A HUD may be used off-label in an emergency situation, i.e., to save the life or protect the physical wellbeing of a patient. The treating physician should ensure that the following patient protection measures are followed before and after the emergency use occurs:

- **Before** the HUD emergency use occurs:
  - If possible, the treating physician should obtain the following:
    - Concurrence of the IRB Chair or IRB Staff;
    - Informed consent from the patient or his/her LAR;
    - An independent assessment by an uninvolved physician; and
    - Authorization from the HDE holder before the emergency use.
- **After** the HUD emergency use:
  - The treating physician must submit a notification to the IRB in writing within five (5) business days of the emergency use of the HUD, which will include:
    - Patient's condition, date of use, and the reason for the use.
  - It is highly suggested that the treating physician also submit a follow-up report to the HDE Holder on the patient's condition.

3.91 Compassionate Use of a HUD (for a Single Patient): Please see IRB SOP 506.

4. RESPONSIBILITY

IRB Manager or staff will review the HUD submission and all supplemental materials submitted by the physician to ensure completeness.

IRB Manager or staff will assign appropriate Primary and Secondary Reviewer and/or obtain appropriate consultant.

IRB Primary and Secondary Reviewer are responsible for the review and presentation of the HUD to the other IRB members.

IRB members are responsible for reviewing and conducting a thorough discussion of the HUD application.

5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 814 Subpart H
21 CFR 814.124
FDA Humanitarian Device Exemption (HDE) Program Guidance for Industry and Food and Drug Administration Staff

6. REFERENCED DOCUMENTS

A list of approved HDEs along with the approval order, summary of safety and probable benefit, labeling and patient information is available at:
https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/HDEApprovals/ucm161827.htm

REVISION HISTORY

Revision Number	Version Date	Approved By	Date Approved
3.0	11/4/2020	Avera Institutional Official	12/4/2020
• Added a new section (3.8) regarding use of a HUD outside of the FDA approved indications.			
2.1	6/30/2020	Avera Institutional Official	9/22/2020
• Changed a HUD designation to be less than 8,000 people in U.S., instead of 4,000 people. • Added CITI HUD module training requirement. • Added PI must sign the Humanitarian Use Device (HUD) Lead Clinician Roles and Responsibilities - Acknowledgement Form. • Added a link to the FDA's list of approved HDE's. • Added that the physician needs to submit a closure to the IRB. • Since there is an IRB Compassionate Use SOP (#506), referred the user to this SOP instead of summarizing it here.			
2.0	7/16/2019	Avera Institutional Official	7/23/2019
• Explained that a device sponsor must complete a Humanitarian Device Exemption (HDE) application with the FDA in order to be considered for HUD status. • Stated that per regulations, the IRB has the discretion to determine the conditions of HUD use. The IRB may approve the use of the device in general, in a specific number of patients, only under specific circumstances, etc. • The IRB may require the use of an informed consent or may determine that the product labeling developed by the HDE holder incorporates enough information to assist a patient in making an informed decision about the use of the device. • Continuing review of a HUD may be done at the expedited review level. • A physician must notify the IRB of an Emergency use of a HUD within five (5) days of use. • Other administrative edits.			
1.0	August 2016	Director HSRP	August 2016