| University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures | | | |
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| **Revision #4** | **TITLE: Humanitarian Use Device (HUD)** | | **Page 1 of 7** |
| Approved By: ORI Director | Signature | Date | Date First Effective: 07-24-06 |
| Approved By: Nonmedical IRB Chair | Signature | Date | |
| Approved By: Medical IRB Chair | Signature | Date | Revision Date: 05-09-19 |

## OBJECTIVE

To describe the process for Institutional Review Board (IRB) review of a humanitarian use device (HUD) including clinical, emergency, compassionate, and investigational use

## GENERAL DESCRIPTION

The University of Kentucky (UK) Medical IRBs may approve the following situations involving HUDs:

- Clinical use of a HUD as a legally marketed device; OR
- Emergency or compassionate use of a HUD based on a healthcare provider/principal investigator (PI) request that meets IRB criteria; OR
- Investigational use for research purposes either consistent with approved labeling or off-label.

*Definitions*

A *Humanitarian Use Device* is a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 8,000 individuals in the United States per year.

The term *Use* refers to use of a HUD according to its approved labeling and indications.
The term *Investigational Use* refers to research involving a HUD.

A *Humanitarian Device Exemption* (HDE) is a Food and Drug Administration (FDA) marketing application that is similar to a premarket approval application but is exempt from the effectiveness requirements of the medical device law, provided the device meets safety conditions and will not expose patients to significant or unreasonable risk. An HDE approval is based on safety and probable benefit.

An *Investigational Device Exemption* (IDE) refers to the regulations under 21 CFR 812. An approved IDE means that the IRB (and FDA for significant risk devices) has approved the sponsor's study application, and the proposed use meets all the requirements of 21 CFR 812.

## RESPONSIBILITY

Execution of SOP: IRB, IRB Chair, IRB Vice Chair, IRB Members, Office of Research Integrity (ORI) Staff, Principal Investigator (PI)/Study Personnel, Healthcare Providers

## PROCEDURES

*HUD Clinical Use for Treatment or Diagnosis Consistent with Approved Labeling*

Before use of the HUD, the responsible healthcare provider submits an IRB application to the ORI in accord with the Initial Full Review SOP for review and approval by the IRB.

1. The convened Medical IRB reviews clinical use of a HUD, using all standard full review criteria and procedures.

2. The IRB approves the clinical use of the HUD device consistent with the scope of the FDA-approved labeling for groups of patients who meet the clinical criteria.

3. The IRB may choose to require informed consent or allow use of a modified clinical consent that is consistent with or combined with the approved labeling and/or patient information packet.

4. When the healthcare provider submits Continuation Review (CR) materials, the Medical IRB conducts continuing review using standard criteria and procedures. The IRB may use expedited review procedures for continuing review.

5. The healthcare provider submits a report to FDA and to the IRB whenever 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 (21 CFR 814.126(a)).

6. The healthcare provider labels and stores the HUD in a secure manner to ensure appropriate accountability and traceability and to clearly display any use limitations or restrictions designated by the IRB or HDE holder.

*HUD Emergency Use for Both Off-Label or Approved Label Use*

1. The healthcare provider submits an emergency use request directly to the IRB Chair in accord with the Emergency Use SOP. However, if the immediate use of the HUD is, in the healthcare provider's opinion, required to preserve the life of the patient and time is not sufficient to obtain assessment by the IRB chair or designee, the healthcare provider submits a report in writing within five (5) working days following the use as described in #2 below.

2. The Medical convened IRB, IRB Chair, Vice Chair, or medically qualified IRB member assesses the request to determine whether it meets the following regulatory requirements for emergency use of a HUD in a single subject:
    - The patient has a life-threatening condition; OR
    - The patient has a serious medical condition that can reasonably be expected to benefit from the use of the HUD; AND
    - This is the best acceptable treatment alternative for the patient; AND
    - Alternative treatments pose greater risks for the patient or are deemed to provide less benefit than the HUD.

3. The healthcare provider obtains informed consent from the patient or the patient's legally authorized representative using the IRB-approved consent form or modified clinical consent that is consistent with or combined with the approved labeling and/or patient information packet.

4. If the healthcare provider proposes to administer the HUD in emergency use situations without informed consent, the request to the IRB Chair includes a statement certifying in writing that the proposed use meets all of the conditions listed in 21 CFR 50.23. If possible, this statement should include an assessment from an independent physician who is qualified in the appropriate medical specialty. However, if the immediate use of the HUD without informed consent is, in the healthcare provider's opinion, required to preserve the life of the patient and time is not sufficient to obtain the independent determination by a qualified physician, the independent evaluation must be included in writing in the report provided within five (5) working days as described in #5 below.

5. Within five (5) working days following the emergency use, the healthcare provider submits written notification of the use to the IRB including identification of the patient involved, the date of use, and the outcome of the administration. The convened IRB reviews the report consistent with procedures in the Emergency Use SOP.

6. If the healthcare provider fails to submit a request involving emergency use of an HUD to the IRB for review and confirmation prior to initiation, the IRB retrospectively reviews the

information pertaining to the situation to determine if the administration met the regulatory definition of HUD use and whether failure to comply with this SOP meets the IRB definition of noncompliance. (See the Noncompliance SOP.)

7. If the healthcare provider administering the emergency use HUD is not listed on the IRB approved HUD protocol, he/she identifies and informs the principal healthcare provider on the protocol within five (5) working days of the emergency use.

8. For emergency use of a HUD, the healthcare provider assumes the responsibilities of the HDE holder, monitors the patient, and reports the use of the HUD (including any safety-related information) to the HDE holder or FDA.

9. The healthcare provider submits a report to the HDE holder or FDA and to the IRB whenever 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 (21 CFR 814.126(a)).

*HUD Off-Label Clinical Use for Treatment or Diagnosis*

1. FDA determines safety and probable benefit for use of a HUD within its approved indications.

2. If a healthcare provider proposes clinical use of a HUD outside of the approved indications, he/she contacts the HDE holder to determine if any requirements or restrictions exist that prohibit off-label use.

3. Before use of the HUD, the healthcare provider proposing the off-label clinical use protocol submits an IRB application to the ORI in accord with the Initial Full Review SOP for review and approval by the IRB.

4. The healthcare provider includes the following with the Medical IRB submission:
    a. HDE holder documentation allowing off-label clinical use (if available) or attestation that use does not violate existing restrictions or limitations;
    b. Justification for off-label clinical use;
    c. Circumstances which necessitate treatment using the HUD;
    d. A discussion of why alternative treatments are unsatisfactory; and
    e. Assurances and information about patient protection measures.

5. In the title of the application, the healthcare provider includes the words "Off-label Use HUD". The convened Medical IRB reviews the off-label clinical use using all standard full review criteria and procedures.

6. The healthcare provider obtains informed consent from the patient or the patient's legally authorized representative using the IRB-approved consent form or modified clinical consent that is consistent with or combined with the approved labeling and/or patient information packet.

7. When the healthcare provider submits Continuation Review (CR) materials, the Medical IRB conducts continuing review using standard criteria and procedures. The IRB may use expedited review procedures for continuing review.

8. The healthcare provider submits a report to FDA and to the IRB whenever 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 (21 CFR 814.126(a)).

9. The healthcare provider labels and stores the HUD in a secure manner to ensure appropriate accountability and traceability and to clearly display any use limitations or restrictions designated by the IRB or HDE holder.

*Off-Label Single-Subject Compassionate Use*

1. A healthcare provider with an IRB approved HUD protocol may request a protocol exception for a single-subject compassionate use in accord with the Deviations and Exceptions SOP.

2. The healthcare provider includes the following in the exception request:
   - HDE holder documentation allowing off-label compassionate use (if available) or attestation that use does not violate existing restrictions or limitations;
   - Justification for off-label clinical use;
   - A description of the patient's non-emergent condition and the circumstances necessitating treatment with the device;
   - A discussion of why alternative treatments are unsatisfactory; and
   - Assurances and information about patient protection measures.

3. The IRB Chair, other IRB member, or convened IRB conducts the review in accord with the Deviations and Exceptions SOP.

4. The healthcare provider monitors the patient and submits a follow-up report including any safety-related information to the HDE holder or FDA and IRB.

5. The healthcare provider submits a report to the HDE holder or FDA and to the IRB whenever 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 (21 CFR 814.126(a)).

*HUD Investigational Use Consistent with Labeling*

1. The IRB may, at its discretion, approve a PI's application for the investigational use of a HUD to collect safety and effectiveness data consistent with the scope of the FDA-approved labeling.

2. The PI conducting an investigation of a HUD according to its approved labeling and indication must obtain IRB approval and informed consent consistent with all FDA-regulated clinical studies. Hospital consents are not sufficient for investigational use.

3. The PI submits an IRB application to the ORI and the IRB reviews and approves the study in accord with the Initial Full Review SOP.

*HUD Off-Label Investigational Use*

1. The IRB may, at its discretion, approve a PI's application for the investigational use of a HUD beyond its approved labeling when the proposed use is in compliance with 21 CFR 812 requiring an IDE, if there is significant risk.

2. The PI submits an IRB application to the ORI and the IRB reviews and approves the study in accord with the Initial Full Review SOP and the Medical Device SOP.

3. The ORI and IRB follow procedures outlined in the Medical Device SOP for IRB review of significant risk and non-significant risk investigational device use. (See Medical Device SOP.)

4. If the HUD carries significant risk, the PI may conduct the study following FDA approval of an IDE application.

5. The PI obtains informed consent consistent with all FDA-regulated clinical studies. Hospital consents are not sufficient for investigational use.

**REFERENCES**


21 CFR 812
21 CFR 814
21 CFR 50.23
FDA HUD Designation based on 21st Century Cures Act


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