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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: 07-20-11

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 4,000 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.

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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

1. The healthcare provider responsible for the use of the HUD submits an IRB application to the ORI in accord with the Initial Full Review SOP. He/she obtains IRB approval before use.
2. The full Medical IRB reviews clinical use of a HUD in a convened meeting using all standard full review criteria and procedures. The IRB approves the use of the HUD device consistent with the scope of the FDA-approved labeling for groups of patients meeting clinical criteria.
3. The IRB may choose to require informed consent or allow use of a modified clinical consent or operative permit that is consistent with the approved labeling.
4. The healthcare provider seeks and the Medical IRB provides 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.

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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, then the healthcare provider submits a report in writing within five working days as described below.
2. The Medical 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 or operative permit.
4. If the healthcare provider proposes to administer the test article 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 qualified physician, then the independent evaluation must be included in writing in the five working days report described below.
5. Within five working days of 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 investigational test article to the IRB for review and confirmation prior to initiation, the IRB retrospectively reviews the situation to determine if the test article administration met the

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regulatory definition 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 clinician on the protocol within five working days of 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 Compassionate Use Off-Label Use

1. The healthcare provider submits an IRB application to the ORI.
2. In the title of the application on the General Information Sheet, the healthcare provider includes the words: "Compassionate Use HUD."
3. The UK IRB may, at its discretion, approve a healthcare provider's application for the compassionate use of a HUD when the proposed use meets the following criteria:
 - The healthcare provider has determined that there is no alternative device for the patient's condition; use does not violate existing restrictions or limitations; and there is no emergency.
 - The healthcare provider has provided the HDE holder and the Medical IRB with the following:
 - A description of the patient's 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.
4. The healthcare provider provides the Medical IRB with information addressing the criteria listed in item 3.
5. In addition, the healthcare provider contacts the HDE holder to determine if any additional requirements or restrictions exist prior to use.

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6. The full IRB reviews compassionate use in a convened meeting using all standard full review criteria and procedures. The approval applies to the single case requested and does not apply to a class of patients.
7. 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 or operative permit.
8. The healthcare provider monitors the patient and submits a follow-up report 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 Investigational Use Consistent with Labeling

1. The UK IRB may, at its discretion, approve a PI's application for the investigational use of a HUD device to collect safety and effectiveness data consistent with the scope of the FDA-approved labeling.
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.
3. 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 or operative permits are not sufficient for investigational use.

HUD Off-Label Investigational Use

1. The UK IRB may, at its discretion, approve a PI's application for the investigational use of a HUD device beyond its approved labeling when the proposed use is in compliance with 21CFR 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.)

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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 or operative permits are not sufficient for investigational use.

REFERENCES

21 CFR 812.35(a)
21 CFR 814
21 CFR 50.23