

**INSTITUTIONAL REVIEW BOARD (IRB) SUMMARY
MEDICAL DEVICES: HUMANITARIAN USE DEVICES**

(Source: [21 CFR PARTS 20 AND 814 SUBPART H 814.124](#) and [2010 FDA HUD Guidance](#))

- ◆ A **humanitarian use device** (HUD) is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year.
- ◆ A HUD can be approved for marketing through a **humanitarian device exemption** (HDE). Unlike the premarket approval application (PMA), the HDE does not require clinical data demonstrating effectiveness. However, the HDE must contain sufficient information for the Food and Drug Administration (FDA) to determine that the probable benefit to health outweighs the risk of injury or illness.
- ◆ UK IRB requirements and procedures for use of a HUD are outlined in the [IRB Humanitarian Use Device \(HUD\) Standard Operating Procedure \(SOP\)](#)

HUD USE

General Requirements

- ◆ The term “**use**” refers to the use of a HUD for clinical care according to its approved labeling and indication. FDA has decided that a HUD which provides for marketing approval, does not constitute “research” or an “investigation”, however FDA has determined that clinical use of a HUD requires prospective IRB review and approval.
- ◆ Because a HUD is a legally marketed device, no systematic data is collected; however Medical Device Reporting (MDR) reports may provide risk and benefit information for continuing review.
- ◆ For many HDEs, the HDE holder is required to provide training on the use of the device prior to the health care provider using the device. Such requirements would be specified in the HDE approval order, available at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfHDE/HDEInformation.cfm#2>.
- ◆ The healthcare provider responsible for the IRB approved HUD device should clearly label and store the device to ensure accountability and traceability and prevent use outside of designated sponsor or IRB restrictions/ limitations.

IRB Review

- ◆ As stated in [21 CFR 814.124\(a\)](#), the humanitarian device exemption (HDE) holder must ensure that the HUD is administered only to patients at health care facilities having a duly constituted IRB as outlined in the FDA IRB regulations (21 CFR Part 56). The health care provider at such facilities is responsible for obtaining IRB approval before use of the HUD.
- ◆ Initial IRB approval should be performed at a convened IRB meeting and continuing review of the HUD is required in accord with IRB regulations 21 CFR Part 56. FDA allows continuing review to be conducted using the expedited review procedures (see 21 CFR 56.110) unless the IRB determines that full board review should be performed.
- ◆ The IRB must have among its members (or consultants) the appropriate expertise to perform an adequate review of the use of a HUD at the institution. IRBs may defer in writing to another similarly constituted IRB that has agreed to assume responsibility for initial and continuing review of the use of the devices.
- ◆ The IRB does not have to review and approve each individual use of the HUD. The IRB may approve the use of the device in general, for groups of patients clinically appropriate for the device’s intended use.

- ◆ The IRB may consider the health care provider's qualifications through training and expertise with use of the device. The IRB may place limitations on the use of the device based upon: (1) one or more measures of disease progression; (2) prior use of and failure of the alternative treatments; (3) reporting requirements to the IRB or IRB Chair; (4) appropriate follow-up precautions and evaluations, or; (5) any other criteria IRB determines to be appropriate.

Informed Consent

- ◆ Since use of a HUD according to its approved labeling is not research, FDA waives the requirements for informed consent. State law or local institutional policy may require informed consent. The IRB may choose to require informed consent when the IRB approves use of the HUD in a facility.
- ◆ If Informed consent is required, the form or process may include information from the HDE holder's patient information packet found at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfHDE/HDEInformation.cfm#2>. If no packet is available, suggested content includes explanation that the HUD is designed to diagnose or treat the disease or condition described in the HDE labeling 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; a description of the use of the HUD; all known risks or discomforts; an explanation of the postulated mechanism of action of the HUD in relation to the disease or condition; a statement indicating that the effectiveness of this device for this use has not been demonstrated; and a statement that the patients information may be shared with a sponsor or FDA. The IRB may decide to include other information.
- ◆ Even when the IRB does not require informed consent, the healthcare provider should provide patients receiving HUD with information from the HDE holder's patient information packet which may be obtained by selecting the HDE number on the [FDA website](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfHDE/HDEInformation.cfm#2) (<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfHDE/HDEInformation.cfm#2>).

EMERGENCY AND COMPASSIONATE USE OF A HUD OUTSIDE APPROVED INDICATIONS

- ◆ Physicians should be cognizant that FDA has made a determination of safety and probable benefit for use of the HUD only within its approved indication(s). If a HUD is used outside its approved indication(s) in an emergency or compassionate situation, the FDA recommends that the physician obtain informed consent from the patient and ensure that patient protection measures are followed.
- ◆ The UK IRB requires prospective IRB review and informed consent in a format appropriate for emergency or compassionate use.
- ◆ For emergency off-label use, the health care provider or investigator follows the same procedures that govern emergency use of an unapproved device; that is obtaining IRB chairperson's concurrence, informed consent from the patient or legally authorized representative; written report submitted to the IRB within five working days of use, and independent assessment by an qualified physician if HUD administered without prior informed consent.
- ◆ For emergency or compassionate use, the healthcare provider monitors the patient and submits a report of use to the HDE holder or FDA, including any safety related information.

HUD INVESTIGATIONS

- ◆ The term, “**investigational use**” is used when a HUD is being used in research to collect safety or effectiveness data.
- ◆ A HDE holder may collect safety and effectiveness data for the HDE-approved indications without an IDE. If the HUD is the subject of a clinical investigation (i.e. safety and effectiveness data will be collected), then IRB approval and informed consent is required because this is an FDA regulated clinical investigation. If the HUD is studied in a clinical investigation, the elements included in the informed consent document must conform to the requirements found in 21 CFR 50.25.
- ◆ Clinical investigations of a HUD beyond its approved indication(s) (e.g. for a broader or different indication) must be conducted in compliance with 21CFR 812 requiring an IDE if significant risk(SR). IRB approval and research informed consent are required.



[FDA DECISION TREE FOR IRB REVIEW OF HUDS](#)

The above link provides guidance based solely on the FDA HUD regulations.

ADDITIONAL HDE REQUIREMENTS

- ◆ Holder of the humanitarian device exemption is required to notify FDA of the withdrawal of approval for a humanitarian use device by an IRB within five working days after being notified of the IRB action.
- ◆ The holder of the HDE may charge for the device if the amount does not exceed the cost of research and development, fabrication, and distribution except under certain pediatric indications. If a HUD is studied in a clinical investigation of a new indication, the HDE holder may not charge subjects or investigators a price larger than necessary to recover manufacturing and handling costs.
- ◆ Device user facilities and/or manufacturers are required to submit a report to FDA and to the IRB of record including 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)). Serious injury means an injury or illness that (1) is life-threatening, (2) results in permanent impairment of a body function or permanent damage to a body structure, or (3) necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure (21 CFR 803.3).

HIPAA

- ◆ The use of a HUD according to its approved labeling and indication is generally for treatment or diagnosis, even though such use requires IRB approval. If a HUD is being used according to its approved labeling and indication for treatment purposes, and not in a clinical investigation, then protected health information about a patient may be used or disclosed for treatment or diagnostic purposes without the patient’s authorization under HIPAA.
- ◆ If a HUD is being used in a clinical investigation for research purposes, whether or not the use of the HUD is the subject of the investigation, then protected health information about a patient that is used or disclosed for purposes of the clinical investigation requires the patient’s authorization under the HIPAA Privacy Rule. The IRB may waive this authorization if certain waiver criteria are met.

SUMMARY OF FEDERAL AND INSTITUTIONAL HUD REQUIREMENTS

The table below summarizes requirements based on FDA guidance and UK Institutional Policy.

For details see the [UK HUD SOP](#).

Condition	Regulatory Approval	IRB Approval Requirement(s)	Single case or Group Approval	Informed Consent Requirement
HUD Use (on label)	FDA approved for marketing under Humanitarian Device Exemption (HDE)	The healthcare provider must obtain IRB approval before use of a HUD.	IRB may approve the use of the device within the scope of the FDA-approved indications for groups of patients meeting clinical criteria.	FDA does not require informed consent for use of a HUD. 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.
Emergency Use HUD	Healthcare provider assumes patient monitoring responsibilities of HDE holder, and reports the outcome of the emergency use including any safety related information to the HDE holder or the FDA.	UK policy requires prior review and confirmation that the case meets emergency use criteria by the IRB Chair or designee. MD also must submit to the IRB a follow up report within five working days of emergency use.	Single case	UK policy requires informed consent be obtained from patient or legally authorized representative (LAR) using IRB approved consent form or modified clinical consent or operative permit. Consistent with the UK Emergency Use SOP, if emergency situation requires use without informed consent, independent assessment from a qualified physician is required.
Compassionate Use HUD (outside approved indication)	Healthcare provider contacts the HDE holder to determine any restrictions and reports the outcome of the compassionate use, including any safety related information, to the HDE holder or FDA.	The healthcare provider must obtain approval for HUD Compassionate Use from full IRB.	Single case	Informed consent from patient or LAR is required using IRB approved consent form or modified clinical consent or operative permit.
Investigational Use of a HUD according to its approved labeling and indications	A HDE holder may collect safety and effectiveness data for the HDE-approved indications without an IDE.	The investigator must obtain IRB approval for a HUD Investigation	Either per protocol	Research informed consent is required as this is an FDA regulated investigation.
Investigational Use of a HUD beyond its approved indication (new indication)	An investigation of a HUD for a different indication must be conducted in compliance with the IDE regulations 21 CFR Part 812.	The investigator must obtain IRB approval for a HUD Investigation. The IRB will need to make a SR/NSR determination, unless already determined by FDA.	Either per protocol	Research informed consent is required as this is an FDA regulated investigation.

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Based upon:

Department of Health and Human Services, Food and Drug Administration, 21 CFR Parts 20 and 814

Department of Health and Human Services, Food and Drug Administration, SUBPART H – HUMANITARIAN USE DEVICES 814.100

FDA [Final Guidance](#) for HDE Holders, Institutional Review Boards (IRBs), Clinical Investigators, and FDA Staff

Humanitarian Device Exemption (HDE) Regulation: Questions and Answers, July 8, 2010