# PURPOSE

## This document describes the policies and procedures about medical devices that have been classified by the Food and Drug Administration (FDA) as humanitarian devices (HUDs).

# POLICIES

## The UW applies the regulations of the Food and Drug Administration (FDA) when clinicians use a Humanitarian Use Device (HUD). This includes the requirement to obtain prospective IRB approval and ongoing review (except in emergency situations), even though the clinical use of a HUD is not considered to be research.

## The UW IRB requires that documented consent be obtained from patients for the use of a HUD whenever possible.

## The UW IRB does not make any distinction between the “on-label” versus the “off-label” use of a HUD. Such distinction is not required by FDA policies and regulations related to HUDs.

## UW policies about the procedures required for the uses of HUDs are summarized here:

### Clinical emergency use (on-label or off-label)

#### If the HUD has already been approved by the UW IRB ([see this list](https://www.washington.edu/research/hsd/guidance/humanitarian-use-devices/)): No interaction with HSD or the IRB is required.

#### If the HUD has not been approved by the UW IRB: Follow the instructions in **INSTRUCTIONS and NOTIFICATION Emergency Use, Device**.

### Clinical non-emergency use (on-label or off-label)

#### If the HUD has already been approved by the UW IRB ([see this list](https://www.washington.edu/research/hsd/guidance/humanitarian-use-devices/)): No interaction with HSD or the IRB is required.

##### If repeated off-label uses are expected and they were not described in the application reviewed by the UW IRB: It is best practice to modify the existing application for general off-label use. This does not require approval from the FDA.

#### If the HUD has not been approved by the UW IRB: Submit an IRB application in the Zipline system.

### Research use (e.g., collecting safety and effectiveness data)

#### IRB approval must be obtained in advance, even if the HUD is already approved by the IRB for clinical use at the UW.

#### If the research involves using the HUD for its HDE-approved indication (i.e., on-label): It is not necessary to obtain an IDE from the FDA.

#### If the research involves using the HUD “off label”: An IDE must be obtained from the FDA.

## Continuing review of the use of HUDs may be conducted by the expedited review process, if deemed appropriate by the IRB and the HUD is being used solely for clinical purposes.

# DEFINITIONS

## Humanitarian use device (HUD). A HUD is a device that is 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. HUDs can be used (i.e., marketed) without having been shown to meet the standard effectiveness criteria applied to other devices. Clinical use of a HUD is not considered to be research, but the FDA nonetheless requires IRB review prior to use.

## Humanitarian device exemption (HDE). The term “HDE” refers both to a type of application submitted to the FDA and also to the FDA’s approval of the application. A HDE application to the FDA is not required to provide research data demonstrating that the device is effective. However, it must contain sufficient information for the FDA to determine that the probable health benefit outweighs the risk of injury or illness, that the device will not expose patients to unreasonable or significant risk, and that there is no comparable device available to treat or diagnose the disease or condition. An approved HDE authorizes marketing of a HUD.

## HDE holder. The person who obtains the approval of a Humanitarian Device Exemption (HDE) from the FDA. Once the HDE is approved, the HDE holder is responsible for ensuring that the HUD is used only under the review and oversight of an IRB.

# RESPONSIBILITIES

## The responsibilities of the physician and the IRB are outlined below.

# PROCEDURES: Clinical Use of a HUD

## Initial IRB review (21 CFR 814.124)

### Applicable regulations. FDA regulations require standard IRB review, even though clinical use is not considered a research activity. The IRB must be constituted and act in accord with the FDA regulations governing IRBs, even though this is clinical care and not research (21 CFR 56; see **SOP IRB Review** and **WORKSHEET IRB Review Outcomes**).

#### Note that if safety and effectiveness data are being collected, the use is considered research rather than clinical care.

### Full convened review. The FDA requires the initial review and approval to be conducted by the full convened IRB.

### What is reviewed. It is UW IRB policy to require the physician to provide the following materials for the IRB to review. Other items commonly included with an IRB application are not required (e.g., HIPAA authorization form).

#### A standard IRB application form, completed as applicable for the clinical care situations. This should include a description of how the physician proposes to use the device, including a description of any screening procedures, the HUD procedure, and any patient follow-up visits, tests, or procedures, as well as which physicians may use the device.

#### The Device Supplement to the application.

#### The consent form that will be used with the patients.

#### Copy of the HDE approval document from the FDA.

#### The product labeling information.

#### The Patient Information Sheet/Packet, if there is one.

#### Photo or drawing of the device, and any description information.

### Criteria for approval. The FDA recommends (reference 9.5) that an IRB apply the review criteria described at 21 CFR 56.111 and elsewhere in FDA regulations Part 56 “as much as possible”. The UW IRB’s interpretation of this recommendation is indicated below in Section 10 by re-printing the criteria and striking through the specific sections that the UW does not apply. In addition, the UW IRB must be satisfied that the use of the HUD is for clinical care only, and is not being used for research purposes.

### What is approved. The IRB is not required to review and approve each individual use of a HUD, but rather the IRB may approve use of the device as it sees fit as long as the approval period is no longer than one year long. For example, the FDA states that the IRB may specify limitations on the use of the device based on:

#### Measures of disease progression.

#### Prior use and failure of any alternative treatments.

#### Reporting to the IRB, the IRB Chair, or other appropriate IRB member.

#### The outcome of follow-up precautions and evaluations.

#### Any other criteria it determines are appropriate.

### Financial charges to the patient. The FDA allows the patient to be charged for the HUD within certain constraints. The FDA monitors the HDE holder on this issue. The IRB neither reviews any charges nor requests justification for them.

### IRB approval period. Identification of the IRB approval period follows the same considerations and requirements as an IRB review of research. That is, the period may not exceed one year.

#### If the risk of the device warrants it, the IRB may approve shorter approval periods, or it may approve the HUD for a specific number of patients and require a summary report before approving the use in additional patients (as long as the review occurs within one year of the initial approval).

### Number of patients. It is the responsibility of the HDE holder, not the IRB, to monitor how many HUD devices are distributed each year in the U.S. “Over-enrollment” of the number of HUDs used clinically at the UW is not defined by the UW as noncompliance.

## Consent requirement

### Applicable regulations. The FDA and its HDE regulations do not require informed consent as defined by the FDA’s research regulations (i.e., 21 CFR 50; see reference 7.5). Because the HDE means that the device is approved for marketing, the use of the HUD does not constitute research and therefore does not require a research consent from study subjects.

### UW policy. However, it is UW policy to require documented consent from patients prior to the use of a HUD, whenever possible.

#### The physician should obtain the HUD consent using the following materials provided to the patient:

##### Any Patient Information Packet prepared by the HDE holder. (Most HDE holders develop patient information packets that generally contain a discussion of the potential risks and benefits of the HUD and any procedures associated with its use).

##### A consent form, with the following information:

###### An explanation that the HUD is designed to diagnose or treat the disease or condition described in the HDE labeling.

###### No comparable device is available to treat the disease or condition.

###### 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 sentence indicating that although the device is authorized by Federal law, the effectiveness of the device for this use has not been demonstrated.

#### The required elements for a research consent are not required for a HUD consent.

#### The criteria the IRB uses to assess the consent form and process are:

##### Sufficient information is provided.

##### Patients or their representatives will be given sufficient opportunity to consider whether or not to receive/use the HUD.

##### Information regarding the HUD will be communicated in language understandable to the patient.

## Device risk determination. Because the use of a HUD is not research, the IRB is not required to determine whether the device is “significant risk” or “non-significant risk”.

## HIPAA authorization. Because the use of a HUD is not research, the UW IRB **research** HIPAA Authorization form is not required and should not be used. The UW IRB expects that appropriate HIPAA notifications and clinical authorizations will have already been obtained through the standard UW Medicine process used with all patients.

## Radiation Safety. Because the clinical use of a HUD is not research, any use of procedures involving radiation exposure that is necessary in connection with the HUD does not require review and approval of the UW Radiation Safety Committee.

## UW Medicine requirement. HUDs cannot be used until UW Medicine has notified its Medicare Contractor of the intended use. This is necessary in order to obtain reimbursement for the use (and sometimes for the entire inpatient admission that was required in order to use the HUD). It is the physician’s responsibility to contact the UW Medicine Compliance or billing office for this purpose.

## Vulnerable population determinations. Because the clinical use of a HUD is not research, the IRB is not required to make any regulatory determinations concerning the use of vulnerable populations.

## Compensation for injury language. The clinical use of a HUD is not covered by the UW compensation for injury program.

## Continuing review. Continuing review must follow the procedures and requirements described by the FDA in its clinical investigation regulations (21 CFR 56), even though the use of a HUD is not considered research. See **WORKSHEET Expedited Review**.

### It is UW policy that the IRB should decide as part of its initial review whether subsequent continuing review may be conducted by the expedited review process (see **WORKSHEET Expedited Review**), keeping in mind the requirement for at least one reviewer with appropriate expertise.

#### The FDA believes that expedited review is appropriate (but not required) since the initial review would have been performed by the full IRB and the clinical use of the HUD does not constitute research.

#### The IRB may decide that subsequent continuing reviews of an HUD may occur by the expedited review process only if the HUD is being used solely for clinical purposes.

## Modifications. FDA regulations do not require that changes in the **clinical** use of an IRB-approved HUD (procedures, population, purpose, consent form) be approved in advance by the IRB.

### However, it is best practice to modify the IRB application for broadening the clinical purpose for which an approved HUD is used at UW Medicine, if physicians expect that they will repeatedly use an approved HUD beyond the purpose(s) described in the initial IRB application. This does not require FDA approval.

## Reporting of adverse events

### FDA regulations require the HUD user (i.e., the physician) and the HDE holder to provide adverse event reports to the FDA and to the IRB.

### This is typically accomplished via the Medical Device Reporting (MDR) system.

### HDE holder. In addition, manufacturers must submit reports to FDA and 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)).

### Physician. In addition to MDR reports, the physician must provide reports to the IRB whenever a HUD may have caused or contributed to a serious injury.

#### 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.

## Reporting by the IRB. It is UW IRB policy to copy the HDE holder on any communication in which the UW physician is informed that IRB approval has been suspended or terminated.

# PROCEDURES: Research involving a HUD

## **Research** involving a HUD device (for example, research designed to gather safety and effectiveness data about the HUD) must be reviewed and approved by an IRB following standard procedures and FDA regulations.

### IRB approval of the use of a HUD at a facility to treat or diagnose patients is **not** the same as IRB approval of the investigational use of the HUD (i.e., in research) for the collection of safety and effectiveness data.

## If the research involves a HUD use within the FDA-approved labeling for the HUD.

### Example: a researcher wishes to collect safety and effectiveness data on the FDA-approved use of the HUD.

### An Investigational Device Exemption (IDE) application to the FDA is **not** required.

### Standard prospective IRB review and approval must be obtained.

### Standard research consent must be obtained from the subjects.

### Standard pediatric safeguards, as required by the FDA for any research involving children, must be applied.

## If the research concerns a new use for the HUD (i.e., a use not described on the labeling).

### Example: a researcher wishes to use the HUD for a purpose or population not approved under the HDE, and to collect safety and effectiveness data on that new use.

### An IDE (not HDE) approval must be obtained from the FDA.

### Standard prospective IRB review and approval must be obtained, like any research study, applying all relevant FDA regulations (such as the device risk determination).

### Standard research consent must be obtained from the subjects.

### Standard pediatric safeguards, as required by the FDA for any research involving children, must be applied.

# MATERIALS

## [GUIDANCE Humanitarian Use Devices (HUDs)](https://www.washington.edu/research/hsd/guidance/humanitarian-use-devices/)

## [INSTRUCTIONS and NOTIFICATION Emergency Use, Device](https://www.washington.edu/research/forms-and-templates/instructions-and-notification-emergency-use-device/)

## [SOP IRB Review](https://www.washington.edu/research/policies/sop-irb-review-2/)

## [WORKSHEET Expedited Review](https://www.washington.edu/research/forms-and-templates/worksheet-expedited-review/)

## [WORKSHEET IRB Review Outcomes](https://www.washington.edu/research/forms-and-templates/worksheet-irb-review-outcomes/)

# REFERENCES

## 21 CFR 814 Subpart H (Humanitarian Device Exemption)

## 21 CFR 50 (research informed consent)

## 21 CFR 56 (IRB review of research)

## Humanitarian Device Exemption (HDE) Regulation: Questions and Answers. Guidance for HDE Holders, Institutional Review Boards (IRBs), Clinical Investigators, and FDA Staff. July 8, 2010.

# IRB Approval Criteria for Clinical Use of an HUD

## Risks to patients are minimized: (i) by using procedures whichdo not unnecessarily expose subjects to risk, (ii) whenever appropriate, by using procedures already being performed on the patients for diagnostic or treatment purposes. 21 CFR 56.111(a)(1)

## Risks to patients are reasonable in relation to anticipated benefits. 21 CFR 56.111(a)(2)

### Per UW policy, clinicians are expected to obtain a standard clinical consent that has been appropriately modified to include the following information, whenever possible. If consent is not possible to obtain, the clinician should follow standard UW Medicine policies for how to provide necessary clinical care in the absence of patient consent.

#### A description of the HUD and the reason for using it.

#### A description of any alternatives to using the HUD.

#### A description of the possible risks and benefits of the HUD.

#### A statement that the effectiveness of the HUD has not been fully established.

#### A description of any procedures required to use and monitor the HUD.

### Clinicians are expected to obtain written documentation of the clinical consent, from the patient or the patient’s legal representative, whenever possible. If consent documentation is not possible to obtain, the clinician should follow standard UW Medicine policies for how to provide necessary clinical care in the absence of documentation of patient consent.

## The clinical care plan makes adequate provision for monitoring the safety of patients. 21 CFR 56.111(a)(6)

## There are adequate provisions to protect the privacy of patientsand to maintain the confidentiality of data. 21 CFR 56.111(a)(7)

### The UW IRB assumes that all components of the HIPAA regulations that are relevant to clinical care will be appropriately implemented, following the standard procedures of UW Medicine.

### The UW IRB believes that the clinical care components of HIPAA apply to any records and reports that clinicians are expected to provide about patient outcomes with the HUD to the holder of the HDE and the FDA.

### The UW IRB expects the clinician to follow standard UW Medicine procedures for obtaining consent from patients, including the extra steps that may be required with parents of children, mentally disabled patients, patients with a poor understanding of English, and patients with low education levels.

### Because the use of HUDs is not considered to be research, it is UW policy to not apply all of the subpart D requirements to the use of HUDs in children.

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| **Version Number** | **Posted Date** | **Implementation Date** | **Summary of Changes** |
| 2.2 | 02/25/2021 | 02/25/2021 | Updated HUD definition – manifested in fewer than 8,000 (updated from 4,000 ) per FDA |
| 2.1 | 07/28/2019 | 07/28/2019 | Removed all references to Confidentiality Agreements and to state law RCW 42.48 |
| 2.0 | 05/07/2018 | 05/07/2018 | RE use of HUD: clarified the importance of whether the UW IRB has approved its use, and that it doesn’t matter whether its being used on-label or off-label. Increased version number. |
| 1.5 | 07/26/2017 | 07/26/2017 | Updated links |
| 1.4 | 02/17/2015 | 02/17/2015 | Added link to SOP Device Compassionate Use. Previous versions are beyond record retention. |

**Key Words:** HUD