| Title: HUMANITARIAN USE DEVICE (HUD) | Policy Number: BC-IRB-413<br>Page: 1 of 6 |
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| **SPONSORED BY:** Sponsored Programs and Research Committee | **Issued for:** All BayCare, including without limitation:<br>Bartow Regional Medical Center<br>BayCare Alliant Hospital<br>BayCare Hospital Wesley Chapel<br>Mease Countryside Hospital<br>Mease Dunedin Hospital<br>Morton Plant Hospital<br>Morton Plant North Bay Hospital<br>South Florida Baptist Hospital<br>St. Anthony's Hospital<br>St. Joseph's Hospital<br>Winter Haven Hospital |
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| **Approved by:** Keri Eisenbeis, Chief of Staff<br>**Signature:** | |

This policy is developed as a guideline to address general circumstances. There may be certain instances in which the exercise of professional judgment and/or discretion by the health care provider warrants taking other actions.

**This Humanitarian Use Device (HUD)** Policy applies to BayCare Health System, Inc., and any of its affiliated entities, including those entities listed above (collectively, "**BayCare**").

**SCOPE:**
BayCare Human Research Protection Program

**PURPOSE:**
This policy outlines the BayCare Institutional Review Board (BCHS-IRB) requirements when applying for Humanitarian Use Device (HUD) to BCHS-IRB when BCHS-IRB is the IRB of record. It describes the process for the IRB review of a HUD including clinical, emergency, compassionate, and investigational.

**GENERAL DESCRIPTION:**
IRB approval is required before a HUD is used at a BayCare facility. The only exception to prior IRB approval is an emergency use when IRB approval cannot be obtained in sufficient time to prevent serious harm or death to the patient.

The IRB may use its discretion to determine how and when to approve use of a HUD. The IRB may specify limitations on the use of the device based upon one or more measures of disease progression, prior use and failure of any alternative treatment modalities, and require the Principal Investigator (PI) or treating physician reporting responsibilities to the IRB.

The IRB may approve the following situations involving HUDs:

- **Clinical use of a HUD** as a legally marketed device with approved labeling or off-label; OR
- **Emergency or compassionate use of a HUD** based on a physician/PI request that meets IRB criteria, OR
- **Investigational use** for research purposed either consistent with approved labeling or off-label

**DEFINITIONS / ACRONYMS:**
**HUD – Humanitarian Use Device:** a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than **8,000** individuals in the United States per year as defined in federal statute. HUDs cannot be sold for profit except in narrow circumstances and can only be used in a facility after an IRB has approved their use in that facility, except in emergencies where the physician determines that approval cannot be obtained in time to prevent serious harm or death to the patient. Although the use of a HUD within its approved labeling does not constitute research, the United States Food and Drug Administration (FDA) requires IRB approval to be obtained before a HUD can be used in a facility.

**Compassionate Use:** A HUD is IRB approved and may be used off-label in certain life-threatening situations necessitating the use of the test article.
The physician/PI and an independent physician must conclude that there is no generally recognized standard acceptable treatment or therapy available for use.

**Emergency Use:** A physician, in an emergency, determines that IRB approval for the use of the HUD cannot be obtained in time to prevent serious harm or death to a patient; the HUD may be used within the scope of its labeling or off-label without prior IRB approval.

**HDE – Humanitarian Device Exemption:** An approval process provided by the FDA allowing a medical device to be marketed without requiring evidence of effectiveness. The FDA calls a device approved in this manner a "Humanitarian Use Device" (HUD).

**MDR – Medical Device Reporting**

**Serious Injury** – statutorily defined as 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

**PROCEDURE:**

**1. HUD Clinical Use for Treatment or Diagnosis Consistent with Approved Labeling (On-Label)**

The Physician must obtain IRB approval and institutional clearances prior to first use of the HUD and maintain IRB approval (Continuing Review) for as long as the HUD continues to be used at the institution. Before use of the HUD, the responsible physician submits an IRB application. The IRB conducts a Full Board Review and approval.

***A. IRB Initial Application*:**

HUD initial application includes the following documents:
1. List of all physicians that will use the HUD.
2. Documented approval from impacted departments within BayCare utilizing the clinical research approval form (under research type select HUD)
3. Alongside the submission, research staff provides research Training and Education, Humanitarian Use Devices: Collaborative Institutional Training Initiative (CITI HUD Module) for each physician.
4. The FDA Humanitarian Device Exemption (HDE) Approval Order and product labeling.
5. The HUD brochure and/or the Patient Information Packet, if available.
6. Pertinent information applicable to the HUD.
7. Informed consent form or Patient Fact Sheet for the use of the HUD, is required by the IRB wherever appropriate.
8. Summary of how the physician proposes to use the device, including any screening procedures, the HUD procedure, and any patient follow-up visits, tests, or procedures.

**NOTE:** A physician wishing to use a HUD "on-label" must be individually documented on the physician list provided with Initial submission to obtain IRB approval to use such device. IRB approval for one physician on the facility medical staff does not mean that another member of either the physician's group or facility's medical staff also has approval to use such device. A request to add physicians and/or components/affiliated sites (e.g., hospitals or practice locations) to the same approval require submission to the IRB with an IRB Amendment form via eIRB. Expedited review of such submission is appropriate if the HUD use is within its approved labeling and does not constitute research.
Additionally, the IRB requires specific consent that is consistent with the approved labeling when the IRB approves use of the HUD in a facility. The document must not use the term "research" to refer to the activities associated with this use of the device and the consent form will not need to conform to Human Subjects Research consent regulations.

***B. Continuing Review*:** The physician is required to fulfill continuing review requirements at the designated IRB intervals. At each continuing review, the physician provides the following:
1. The clinical indications for the use of the HUD in each patient/participant.

2. Unanticipated problems involving risk to patients/participants that are possibly related (more likely related than unrelated) to the use of the HUD; and
3. Clinical outcomes of each patient/participant, if known; and
4. HUD Accountability Report

***C. Modifications (Change in Procedure)*:** Modifications to the HUD or proposed changes to the clinical use of the device are promptly submitted to the IRB using the Amendment to Previously Approved form. As applicable, the form is accompanied by; 1) the FDA's approval of the modification and 2) the HDE holder's amendments to the HUD product labeling, HUD brochure and/or other pertinent materials corresponding to the requested modifications including the informed consent form if affected by the change.

***D. Prompt Reporting/Medical Device Reporting (MDR):***
The physician reports any unanticipated problems associated with the use of the HUD in accordance with BC-IRB-411 REPORTING ADVERSE EVENTS INCLUDING SERIOUS ADVERSE EVENTS, UNANTICIPATED PROBLEMS, PROTOCOL DEVIATIONS, VIOLATIONS, or EXCEPTIONS, AND NONCOMPLIANCE Policy. The physician reports to the HDE holder, 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. This HDE regulation requires that MDR reports be submitted to FDA and the IRB.

**2. *HUD Off-Label Clinical Use for Treatment of Diagnosis (Small Group of Patients)***

FDA determines safety and probable benefit for use of a HUD within its approved indications.
If a physician 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.
Before use of the HUD, the physician proposing the off-label clinical use protocol submits an IRB application for review and approval by the IRB. The IRB conducts a full board review of the HUD off-label clinical use application following standard review criteria and procedures.

***A. IRB Initial Application*:**

The physician includes the following with the IRB initial application:
1. HDE holder documentation allowing off-label clinical use (if available) or attestation that use does not violate existing restrictions or limitations
2. Justification for off-label clinical use
3. Circumstances which necessitate treatment using the HUD
4. A discussion of why alternative treatments are unsatisfactory
5. Assurances and information about patient protection measures.

***3. HUD Off-Label Single-Subject Compassionate Use***

A physician with an IRB approved HUD protocol may request a protocol exception for a single-subject compassionate use:
1. The IRB Chair/Vice Chair conducts the review and release concurrence prior to the off-label single-subject compassionate use.
2. The IRB Chair/Vice Chair may concur with a HUD Off-label Single-Subject Compassionate use if he or she agrees with the physician assessment that there is no alternative device for the patient's condition, and that reasonable patient protection measures are taken.
3. If the IRB Chair/Vice Chair does NOT concur with an Off-Label Single-Subject Compassionate use of a HUD, the HUD is not used.

***A. IRB Initial Application*:**

The physician includes the following with the IRB initial application:
1. HDE holder documentation allowing off-label compassionate use (if available) or attestation that use does not violate existing restrictions or limitations
2. Justification for off-label clinical use
3. A description of the patient's non-emergent condition and the circumstances necessitating treatment with the device
4. A discussion of why alternative treatments are unsatisfactory

5. Letter of concurrence from an independent physician stating that there is no generally recognized standard acceptable treatment or therapy available for use
6. assurances and information about patient protection measures.
7. Report 30 day post patient follow-up by submitting closure report to the IRB.

**4. HUD Emergency Use for Both Off-Label or Approved Label Use (On-Label)**

Before HUD Emergency Use for Both Off-Label or Approved Label Use (On-Label), the physician submits the following information to the IRB Office for review and confirmation for emergency use of a HUD in a single subject:

1. IRB application that includes the words "EMERGENCY USE" and the name of the HUD.
2. Physician letter or email with explanation that justifies administration of the HUD Emergency Use, (e.g., life-threatening situation, no standard acceptable treatment available, and not sufficient time to obtain IRB approval); and
3. Copy of the informed consent form.

If the immediate use of the HUD is, in the physician's opinion, required to preserve the life of the patient and time is not sufficient to obtain assessment by the IRB Chair/Vice Chair, the physician submits a report in writing within five (5) working days following the HUD use, as described below in section "C".

The IRB Chair/Vice Chair assesses the request to determine whether the following regulatory requirements for emergency use of a HUD in a single subject are met:

1. The patient has a life-threatening condition; OR
2. The patient has a serious medical condition that can reasonably be expected to benefit from the use of the HUD; AND
3. This is the best acceptable treatment alternative for the patient; AND
4. Alternative treatments pose greater risks for the patient or are deemed to provide less benefit than the HUD.

***A.*** The physician 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.

***B.*** If the physician proposes to administer the HUD in an emergency use situation without informed consent, the request to the IRB Chair includes a statement certifying in writing that the proposed use meets all of the statutorily required conditions. . If possible, this statement includes 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 physician'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 is included in writing in the report provided within five (5) working days as described below in section "F".

***C.*** Within five (5) working days following the emergency use, the physician submits written notification of the HUD use to the IRB. The report includes:
1. A brief description of the life-threatening situation
2. Justification for use of the test article
3. Signed informed consent form or justification for administration without informed consent
4. Statement of review and evaluation of the situation by a physician who is not participating in the clinical investigation (if administered without informed consent)
5. A description of the outcome of administration.

***D.*** If the physician fails to submit a request involving emergency use of a 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 Policy meets the IRB definition of noncompliance.

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

***F.*** For emergency use of a HUD, the physician 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.

***G.*** The physician 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 in accordance with federal statute.

**5. HUD Investigational Use for Both Off-Label or Approved Label Use (On-Label)**

***A. Clinical Investigation*:** For clinical investigations using a HUD, IRB approval is required, and the investigators must adhere to all federal regulations and institutional policies governing human subject research. The PI conducting an investigation of a HUD obtains informed consent consistent with FDA-regulated clinical studies. Hospital consents are not sufficient for investigational use.

***B. Investigational Device Exemption (IDE) Requirements:***

1. ***Investigations that require an IDE:*** When an investigator seeks to collect data for a HUD that is NOT used in accordance with its approved indications (i.e. new use for the device or different indication), then the HUD requires an IDE from FDA and the study follows regulations for IDEs. This requires a significant risk/non-significant risk (SR/NSR) determination by the IRB. If the device is a significant risk device, an FDA approved IDE is required.
2. ***Investigations that DO NOT require an IDE:*** When an Investigator seeks to collect safety and effectiveness data about the HUD, and uses the device within the approved labeling, no IDE is required.

**NOTE:** FDA considers this type of research to be exempt from the requirement for an IDE when the HUD is used in accordance with its approved indications described in labeling. The IRB's review does not need to include a SR/NSR determination if the research is within the HDE-approved indications.

***C.*** 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 federal regulations requiring an IDE, if there is significant risk.

***D.*** The PI submits an initial application to the IRB.

***E.*** The convened IRB reviews the application and provides a determination of SR/NSR for the investigational device use.

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

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

**Referenced Policies**

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| BC-IRB-401 BayCare IRB Initial Approval of Research |
| BC-IRB-405 Requirement for Continuing Review |
| BC-IRB-411 Reporting Adverse Events |

## Appendix 1

This table provides a brief overview of the main differences among the types of Humanitarian Use Device (HUD) cases.

| Type of HUD | Brief Definition | IRB Action | Prior HDE holder or FDA clearance? |
|---|---|---|---|
| **Clinical Use of a HUD (on-label)** | Use of a HUD to **treat or diagnose a patient within the approved labeling and indications.** | IRB Full Board Approval | No |
| **Clinical Use of a HUD (off-label, small group of patients)** | Use of a HUD **to treat or diagnose a patient outside of the approved labeling and indications.** | IRB Full Board Approval | HDE holder |
| **Emergency use of a HUD** | Use of a HUD when an **individual patient is in a life-threatening situation and needs immediate treatment** (there are no alternative options and no time to use existing procedures to get FDA approval for the use) | Chair Concurrence; | No |
| **Compassionate use of a HUD (off-label, single subject)** | Use of an IRB approved HUD to **treat or diagnose an individual patient or a small group of patients** with a serious disease or condition when there are no available alternative options | Chair Concurrence; | HDE holder |
| **HUD Investigational Use (on-label)** | Use of a HUD when **seeking to collect safety and effectiveness data** within the approved labeling and indications. | IRB Full Board Approval | No |
| **HUD Investigational Use (off-label)** | Use of a HUD when **seeking to collect safety and effectiveness data** outside of the approved labeling and indications. FDA approved IDE is required. | IRB Full Board Approval | HDE holder and FDA |