HUMANITARIAN USE DEVICES

4/21/2021

It is the policy of the Duke University Health System Institutional Review Board (DUHS IRB) to review and approve the use of Humanitarian Use Devices. This policy will focus on the following:

1. Definition of terms
2. HUDs used in clinical care
3. HUDs used in a clinical investigation
4. Emergency Use of an HUD
5. Prompt reporting considerations

1. Definition of Terms

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

Humanitarian Device Exemption (HDE): A marketing application for an HUD. An approved HDE authorizes marketing of the HUD. However, an HUD may only be used in facilities having IRB oversight in accordance with 21 CFR Part 56.

Use of HUDs in Clinical Care: Refers to use of the HUD in the course of routine clinical care to treat or diagnose patients (as opposed to approving the "investigational use" or a "clinical investigation" of a device).

Investigational Use or Clinical Investigation: Use in a clinical investigation (collection of safety and effectiveness data). Such use is subject to the same requirements, including 21 CFR 50 and 56, that apply to all FDA-regulated clinical studies.

2. HUDs in Clinical Care

For an HUD to be used for clinical care at DUHS, a Humanitarian Device Exemption (HDE) must be issued by the FDA and the IRB must approve its use at DUHS. While the effectiveness of the device does not have to be demonstrated, the IRB will verify that the device does not pose an unreasonable risk of illness or injury to the recipient, and that the probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. The IRB approval must verify that the use of the HUD, as proposed, is consistent with current labeling of the device and does not exceed the scope of the FDA approved indication.

Note: If the clinician is requesting to use the HUD outside of its current labeled indication and not as part of a clinical investigation, the clinician is required to submit the rationale for using the device off-label. The DUHS IRB will review and determine if the off-label use may be approved within DUHS.

The device's labeling must state that the device is a humanitarian use device and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated.

The initial review of an HUD is to be completed by a convened IRB. Specifically, the FDA recommends reviewing the following materials during initial review of the HUD: a copy of the HDE approval order; a description of the device; the product labeling; the patient information packet that may accompany the HUD; and a summary 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. The IRB may approve use of the HUD without any further restrictions, or under a protocol, or on a case-by-case basis (such as potentially with a request for off-label use).

DUHS IRB will follow the review criteria in 21 CFR 56.111 and elsewhere in part 56, where applicable, including participation of board members with appropriate expertise. The IRB will review the risks to patients that are found in the HDE-approved product labeling, ensure the risks are minimized, and evaluate whether the risks are reasonable in relation to the proposed use of the device at the facility.

Note that FDA regulations do not require informed consent from patients who are treated or diagnosed with an HDE-approved HUD in the course of their clinical care. DUHS IRB will not require that a consent form be submitted for clinical care purposes. However, DUHS IRB does require that patients receive information that includes the following: an 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; and an explanation of the postulated mechanism of action of the HUD in relation to the disease or condition. This may be in the form of an information sheet rather than a consent form. Provision of this information must be documented in the patient's medical record.

The convened Board may make the determination at initial review that continuing review may occur using the expedited procedure if the HUD is not being used in the course of a research study. FDA recommends the use of an expedited procedure because an HDE -approved HUD is a legally marketed device and no safety and effectiveness information is being collected systematically, as would be required for a research protocol. Criteria the IRB may use to grant continuing review using the expedited procedure include: initial use of the HUD was approved without any further restrictions, and the continuing review period was not less than 1 year.

Criteria for subsequent continuing review using the expedited procedure may include: there have been no patient/subject complaints, and no additional risks have been identified.

The IRB may impose more stringent restrictions for use of the HUD as a means of ensuring additional protection, as deemed necessary. For example, the IRB may require re-review at an interval of time more frequent than annually, or may want to conduct re-review after a specified number of patients have been accrued.

When an IRB is deciding whether to approve the use of an HUD at a facility, its review does not include an SR/NSR determination. The use of a legally marketed HUD within its HDE approved indication at a facility to treat or diagnose patients is not a clinical investigation.

When the use of an HUD is for diagnosis or treatment, and not associated with research or data collection, HIPAA regulations for research are not applicable. However, HIPAA regulations for hospital medical records per DUHS institutional policy are applicable.

3. HUDs Used in a Clinical Investigation

Note that FDA regulations and DUHS IRB require that documented informed consent will be obtained from a patient prior to the use of an HUD when the HUD is being used in the course of a clinical investigation (*Per the FDA definition, "Investigation"* means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device).

When an Investigator seeks to collect safety and effectiveness data about the device, if the use is within the approved labeling, no IDE is needed, but IRB approval is required and written informed consent must be obtained since this constitutes research. FDA considers the research to be exempt from the requirement for an IDE as long as the HUD is used in accordance with its approved indication(s). Also the IRB's review need not include a significant risk/non-significant risk (SR/NSR) determination as long as the research concerns the HDE-approved indication(s).

If the Investigator plans to collect data for a new use of the device (a different indication), then the IDE regulations must be followed. If the device is a significant risk device, an FDA approved IDE is required (21 CFR 812). As described previously, IRB approval is required, and informed consent must be obtained, and continuing review by a convened IRB must occur.

For an investigation of the HUD for indications other than the HDE-approved indication(s), the IRB would need to make a SR/NSR determination if that determination has not already been made by FDA. In practice, most sponsors have submitted and obtained FDA approval of an IDE application before submitting such investigations of HUDs to IRBs for review, so IRBs have not needed to make the SR/NSR determination (i.e., FDA had already determined the device was a SR device).

When applicable, review of the use of an HUD and review of the investigational use of an HUD in a clinical investigation may occur simultaneously.

If an HUD is being used in a clinical investigation, whether or not the HUD is the subject of the investigation, then HIPAA regulations for research apply.

4. Emergency Use of an HUD

If a physician in an emergency situation determines that IRB or appropriate local committee approval for the use of the HUD at the facility cannot be obtained in time to prevent serious harm or death to a patient, an HUD may be used without prior approval. In this situation, the HDE holder may ship the HUD, based on the physician's certification of the emergent need and representation that the physician will follow the requirements regarding reporting such use to the chairperson of the IRB or appropriate local committee. The physician must provide notification of the use to the chairperson of the IRB or appropriate local committee, and the notification must include the identification of the patient involved, the date of the use, and the reason for the use. FDA regulations require that physicians provide such notification to the chairperson of an IRB in writing within 5 days of the emergency use of the device.

5. Considerations for Prompt Reporting

Whenever a physician or health care provider receives or otherwise becomes aware of

information from any source that reasonably suggests an HUD has or may have caused or contributed to the death or serious injury of a patient, or has malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur, the physician or health care provider must report such findings to the FDA and the IRB as soon as possible, in keeping with the DUHS IRB's policy on Problems or Events that Require Prompt Reporting to the IRB. 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). This reporting is in addition to, not a substitute for, FDA and/or manufacturer reporting requirements in accordance with 21 CFR 803.

The physician or health care provider shall promptly report any FDA action(s) regarding the HUD to the IRB. Modifications to the HUD or the clinical use of the HUD are to be promptly reported to the IRB in accordance with the IRB policy for Amendments.

References

FDA 21 CFR 814, 21 CFR 803

Humanitarian Device Exemption (HDE) Program Guidance for Industry and Food and Drug Administration Staff; Document issued on September 6, 2019.

https://www.fda.gov/media/74307/download

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