Children's
Healthcare of Atlanta
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Institutional Review Board
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HUMANITARIAN USE DEVICES (HUD) GUIDANCE

Summary:

- Humanitarian Use Device (HUD): A HUD 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"
- Humanitarian Device Exemption (HDE): FDA approval for a physician to use an HUD in clinical treatment or in a clinical investigation. An approved HDE authorizes marketing of an HUD.
- Clinical use of a HUD according to its approved labeling is not research, but the regulations require IRB review.
- The FDA does not required informed consent for clinical use of an HUD; however the IRB may choose to require informed consent or allow use of a modified clinical consent or operative permit. It would be appropriate to include the following statement: *FDA approves HUDs based on safety and probable benefit; however, these devices have not been tested to see how effective they are for your condition.* Even when the IRB does not require informed consent, the provider should provide patients receiving the HUD with information from the HDE holder's patient information packet.
- Use of an HUD for diagnosis or treatment that is not associated with research or data collection, HIPAA regulations for research are not applicable. However, HIPAA regulations for hospital medical records per institutional policy are applicable.
- Research HUD: If the data on the safety and effectiveness of the HUD for the FDA-approved indication to support a Premarket Approval application for the HUD, that may be done under the HDE (rather than an IDE); however, such use of the HUD is considered to be Research and requires submission to the IRB along with a protocol and consent documents. All IRB policies and procedures apply.
- Research HUD: If the Investigator plans to collect data for a new use of the device, then the IDE regulations must be followed, IRB approval is required, informed consent must be obtained, and continuing review must occur using the convened IRB.
- A HUD can be approved for marketing through a humanitarian device exemption (HDE). The HDE does not require clinical data demonstrating effectiveness, but the HDE must provide sufficient information for the Food and Drug Administration (FDA) to determine that the probable benefit outweighs the risk or injury or illness.
- The FDA lists all devices that have been granted an HDE at its Centers for Devices and Radiological Health website at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfHDE/HDEInformation.cfm

HDE Holder Responsibilities:

- For many HDEs, the HDE holder is required to provide training on the use of the device prior to the provider using the device. Requirements can be found in the HDE approval order: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cdHDE/HDEInformation.cfm#2
- The HDE holder must ensure that the HUD is administered only to patients at health care facilities having a duly constituted IRB.
- The HDE holder must notify the FDA of the withdrawal of approval for a HUD by an IRB within five working days after being notified of the IRB action.
- HDE holders may charge for HUDs used clinically to treat or diagnose a patient. If specific eligibility criteria are met, the manufacturer may sell the device for profit within limits. If a HUD is studied in a clinical investigation, the HDE holder may not charge subjects or investigators a price higher than necessary to recover the costs of the HUD.

Physician Responsibilities:

- The physician using the HUD is responsible for providing all applicable information regarding the use of the HUD to the IRB and obtaining IRB approval before the device is used.
- Ensure that a Humanitarian Device Exemption (HDE) exists for use of the HUD and that the proposed use meets the HDE requirements.
- Submit a basic written plan for use of the HUD, HUD manufacturer's product labeling, clinical brochure and/or other pertinent manufacturer information materials, the FDA HDE approval letter, and obtain IRB approval prior to use.
- 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 proven or demonstrated.
- Submit documentation to the IRB for continuing review of the HUD.
- Submit adverse events using the IRB Event Reporting Form. This reporting is in addition to FDA and/or manufacturer reporting requirements in accordance with 21 CFR 803.30.
- 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))
- Obtain consent for Research HUDs or where the IRB has required consent for clinical use of an HUD.

IRB Responsibilities:

- Provide full board initial review of use of the HUD. The IRB may approve use of the HUD without any further restrictions, or under a protocol, or on a case-by-case basis. 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.

- Provide continuing review at the full board or by expedited review at least annually.
- The IRB must ensure that the proposed use is within the FDA-approved indication and that the use of the device does not exceed the scope of the FDA's approval.
- The IRB will verify that the device does not pose an unreasonable risk of illness or injury to the recipient, and that the probably benefit outweighs the risks from use of the device.
- 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 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: one or more measures of disease progression; prior use of and failure of the alternative treatments; reporting requirements to the IRB; appropriate follow-up precautions and evaluations; or any other criteria IRB determines to be appropriate.
- 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.

Emergency Use of HUD:

If a physician in an emergency situation determines that IRB approval for use of the HUD at Children's cannot be obtained in time to prevent serious harm or death to a patient, the HUD may be used without prior IRB approval. The following conditions must be present:

- Patient's life is threatened and patient needs immediate care. The term "life-threatening" is meant to include the presence of serious disease or condition that involves risk of irreversible morbidity, such as loss of eyesight.
- No generally accepted alternative exists.
- There is no time to obtain FDA approval.

If possible, the physician should take as many of the following actions as possible prior to using the HUD:

- Independent assessment of an uninvolved physician.
- Contact the IRB to obtain IRB Chair concurrence for use of the HUD. Notification to the IRB should include identification of the patient involved, date of the use and reason for the use.
- Authorization from the IDE sponsor, if an IDE exists for the device.
- Obtain treatment informed consent for the patient or his/her legally authorized representative and explain to the patient or parent that the HUD is being used for an indication outside the approved labeling
- Provide the patient with the device information packet and an information sheet explaining the FDA's HDE program.
- Develop a schedule to monitor the patient

After use of the device, the following actions should be taken:

- Any of the above actions that did not occur prior to use of the HUD

- No later than 5 business days send a report to the IRB describing the use, reason for the use, and describing patient's current status and protection measures that were followed.
- Provide the IRB with an update and notify the HDE holder of the use and describe patient's current condition
- Monitor the patient according to the identified schedule and report any issues in the use of the device (reportable events, unanticipated problems, etc.) to the HDE holder and the IRB, as appropriate

Compassionate Use:

Compassionate use of an HUD is the "off-label" use of an HUD, or using the HUD for some other diagnosis or condition from which it is intended. If a physician determines there is no emergency, but that there is no alternative to the HUD for the patient's condition and the physician notifies the IRB of the use BEFORE it occurs and obtains IRB approval for the use.

Before using the HUD, the physician using the HUD should take the following actions:

- The physician must contact the HDE holder to determine any restrictions and report the outcome of the compassionate use, including any safety related information to the HDE holder or the FDA
- Provide the HDE holder and IRB with a brief overview of the planned use of the device, identify the patient, why use of the device is necessary the plan for monitoring the patient and obtain full board IRB approval prior to use of the device
- Obtain treatment informed consent for the patient or his/her legally authorized representative and explain to the patient or parent that the HUD is being used for an indication outside the approved labeling
- Provide the patient with the device information packet and an information sheet explaining the FDA's HDE program or include this information in the consent process
- Develop a schedule to monitor the patient

After use of the device, the following actions should be taken:

- Provide the IRB with an update and notify the HDE holder of the use and describe patient's current condition
- Monitor the patient according to the identified schedule and report any issues in the use of the device (reportable events, unanticipated problems, etc.) to the HDE holder and the IRB, as appropriate

References:

21 CFR 814, 21 CFR 803.30
FDA Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors.