SUBJECT: INSTITUTIONAL REVIEW BOARD (IRB) - HUMANITARIAN USE DEVICES

PURPOSE: To define the Children’s Hospital of Wisconsin (CHW) Institutional Review Board (IRB) requirements for review of Humanitarian Use Devices (HUDs).

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I. DEFINITIONS

A. Humanitarian Use Device (HUD) As defined in 21 CFR 814.3(n), 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.”

B. Humanitarian Device Exemption (HDE) A Humanitarian Device Exemption (HDE) is an application that is similar to a premarket approval (PMA) application, but is exempt from the effectiveness requirements of sections 514 and 515 of the Food, Drug, and Cosmetic Act (the Act).
approval of an HDE authorizes an applicant to market a Humanitarian Use Device (HUD), subject to certain profit and use restrictions set forth in section 520(m) of the Act. Specifically, as described below, HUDs cannot be sold for profit, except in narrow circumstances, and they can only be used in a facility after an IRB has approved their use in that facility, except in certain emergencies.

II. POLICY

A. A device manufacturer’s research and development costs could exceed its market returns for diseases or conditions affecting smaller patient populations. The U.S. Food and Drug Administration therefore, developed and published the Humanitarian Device Exemption (HDE) regulation (21 CFR 814) to provide an incentive for the development of Humanitarian Use Devices (HUDs) for use in the treatment or diagnosis of diseases affecting these populations. The regulation provides for the submission by a manufacturer of a HDE application. An HDE application is not required to contain the result of clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for FDA to determine that the device does not pose an unreasonable risk of illness or injury, and that the probable benefit to health outweighs the risk of illness or injury from its use. Additionally, the manufacturer must demonstrate that no comparable devices are available to treat or diagnose the disease or condition, and that they could not otherwise bring the device to market. FDA approval of a manufacturer’s HDE application authorizes marketing of an HUD

B. The FDA requires IRB review and approval for local use of an HUD (21 CFR 814. 124), including Full Committee review and at a minimum, annual continuing review, which may be expedited. This is the only situation where federal regulations require IRB approval and monitoring of an activity that is clearly not research. However, if the HUD is being used in research or in a clinical investigation the IRB must comply with all FDA regulations related to IRB review of research.

C. FDA regulations require that the investigator and/or sponsor clearly state that the device is an HUD and that the effectiveness of the device has not been demonstrated.

D. IRB review of a HUD should include review of the letter or document from the device sponsor that includes the following 10 items:
   1) Generic and trade name of the device
2) FDA HDE #  
3) Date of HUD designation  
4) Indications for the use of the device  
5) Description of the device  
6) Contraindications, warnings, and precautions for use of the device  
7) Adverse effects on health  
8) Alternative practices and procedures  
9) Marketing history  
10) Summary of studies using the device  

The HDE application usually contains this information.

E. FDA regulations do NOT require informed consent to use an HUD, unless the HUD is to be used as part of a research protocol. FDA regulations do not discourage IRBs from requiring informed consent. Many IRBs have required IC stating the unproved status of the device. The Children’s Hospital of Wisconsin IRB has determined that Informed Consent must be obtained from patients or guardians of patients who are to receive an HUD at CHHS facility. In the event the subject is a minor, assent must also be obtained in addition to parent/guardian consent. The consent is to describe the status of the device and the intended use. In addition if an investigator proposes to collect prospective data when the device is used, this data collection should be addressed in the consent. The consent also needs to indicate that the effectiveness of the device for a specific indication has not been demonstrated. The document should not use the term “research” to refer to the use of the device. Unless the purpose of the IRB submission is indeed research. It is also suggested that the investigator provide the HUD brochure (prepared by the manufacturer, if available) to the patient, and review it with the patient prior to use.

III. PROTOCOL SUBMISSION TO THE IRB

An investigator must apply for IRB review before using an HUD at CHW. The materials submitted for review are listed in the HUD/HDE submission checklist. These materials should be submitted to the IRB in the same manner as other research protocols.

A. The protocol submitted to the IRB should contain the following:
   1) Letter or document from the device sponsor that documents the 10 items listed above.  
   2) Summary from the investigator and/or clinician, which describes the intended local use of the HUD. This summary could follow
the format provided in the list referred to above, so that all relevant information about the device and its use is available to the IRB.

3) Marketing materials, brochures, etc. available from the device sponsor.

4) CHW format consent forms for use of the HUD.

IV. CONTINUING REVIEW

Continuing IRB review is required and may occur using expedited procedures if the HUD is not being used as part of a research study. At the time of continuing review, the investigator/clinician must report all HUD uses and activities for the previous year.

V. UNANTICIPATED EVENT REPORTING

Just as with an investigational product, adverse events and unanticipated problems that results from the use of a humanitarian device are subject to “Unanticipated problem” reporting requirements.

FDA regulations require that if a physician or health care provider receives or otherwise becomes aware of information, from any source, that reasonably suggests that a HUD has or may have caused or contributed to the death or serious injury of a patient, the physician or health care provider must report such findings to the FDA as soon as possible, but no later than 10 working days after the Investigator first learns of the effect or problem. This reporting is in addition to, not a substitute for, FDA and/or manufacturer reporting requirements in accordance with 21 CFR 803.30.

VI. USING HUD’s IN AN EMERGENCY USE SETTING

If a physician in an emergency situation determines the use of an HUD outside of the approved indicated use represents an opportunity to prevent serious harm or death to a patient, a HUD may be used in accordance with the emergency exemption procedures (see emergency exemption policies) This use would need to be reported to the sponsor and the investigator is responsible for all reporting as consistent with emergency use procedures.

VII. USE OF A HUD WHEN THERE ARE NO ALTERNATIVES AND IT IS NOT AN EMERGENCY SETTING
If an investigator wants to use a HUD outside its approved indication(s) but it is not an emergency situation, the investigator should contact the IRB office for guidance. Investigators will likely need to submit the same information required for an emergency exemption and also will be required to contact the HDE holder for approval prior to IRB submission for use.

References


Approved By the Institutional Review Board 4/2012