WRIGHT STATE UNIVERSITY

HUD Policy
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Humanitarian Use Device Policy

1.0 Purpose:

For a humanitarian use device (HUD) to be used for treatment as part of clinical care, the HUD must have an approved Humanitarian Use Device Exemption (HDE) from the Food and Drug Administration (FDA) and institutional review board (IRB) approval.

The purpose of this policy is to define Wright State University IRB's submission requirements and approval process associated with HUDs.

2.0 Scope:

This policy applies to the use of HUDs by Wright State University (Wright State) faculty and staff, as well as, when the IRB acts as the IRB of record for HUD approval for an affiliated hospital (i.e., Premier Health, Dayton VAMC).

3.0 Definitions:

3.1 **Research** means a systematic investigation designed to develop or contribute to generalizable knowledge.

3.2 **Human subject** means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) Data through intervention or interaction with the individual or (2) Identifiable private information. [45 CFR 46.102(f)] It is also defined by the FDA to mean an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. [21 CFR 50.4(g) and 21 CFR 56.102(g)].

3.3 **Physician/HUD User (hereafter referred to as "Physician")** means the person(s) who are listed on the IRB of Record approval for the use of the HUD and who are responsible for meeting all requirements pertaining to that use.

3.4 **Clinical Investigation** means any experiment that involves a test article and one or more human subjects and that either is subject to requirements prior to the submission to the Food and Drug Administration (FDA) under section 505(i) or 520(g) or the act, or is not subject to requirements for prior submission to the FDA under these sections of the act, by the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit. [21 CFR 50.3(c) and 21 CFR 56.102(c)]

3.5 **Institutional Review Board (IRB)** means a committee established to review and

approve research involving human subjects. The purpose of the IRB is to ensure that all human subject research be conducted in accordance with all federal, institutional, and ethical guidelines.

3.6 **IRB of Record** means a reviewing IRB that assumes IRB responsibilities and is designated to do so through an approved Federalwide assurance on file with the federal Office for Human Research Protections.

3.7 **Clinical trial** means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

3.8 **Humanitarian Use Device (HUD)** means 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.

3.9 **Humanitarian Device Exemption (HDE)** means a marketing application for a HUD that is exempt from the effectiveness requirements of Sections 514 and 515 or the FD&C Act but subject to restrictions on charges and use. Specifically, HUDs cannot be sold for profit, except in the limited circumstance when indicated for use in children and can only be administered in facilities after IRB approval is obtained, except in certain emergencies. Approval of an HDE requires evidence of safety and probable benefit but does not require establishing effectiveness.

4.0 Policy

The FDA developed and published the HDE regulation (21 CFR 814) to provide an incentive for the development of HUDs for use in the treatment or diagnosis of diseases or conditions affecting smaller patient populations (i.e., not more than 8,000), since manufacturer's research and development costs could exceed its market returns for such devices.

An HDE application must contain sufficient information for the 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.

The use of a HUD within its approved indications is generally not research; it is use of a legally marketed device. For a HUD to be used in treatment or diagnosis, the HUD must have an approved HDE from the FDA and IRB approval. FDA regulations and Wright State require initial IRB review and approval at a convened meeting. Emergency and compassionate use of a HUD may be allowed in accordance with FDA regulations and the *Emergency Use and Research Involving Medical Devices Policy*.

This policy was established to ensure compliance with applicable regulatory requirements and to assist Physicians in understanding when and what information must be submitted to the IRB.

5.0 Procedure

5.1 HUD IRB Application

The Physician is required to submit the following materials to the IRB for review and approval of the use of a HUD:

- HUD application;
- FDA HDE approval order (a list of approved HDEs along with the approval order, summary of safety and probably benefit, labeling and patient information is available at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfHDE/HDEInformation.cfm#2);
- Professional labeling;
- Summary of safety and probable benefit;
- Device manual or brochure (if available);
- Patient labeling/Information Packet (if available);
- HUD Treatment Protocol;
- Consent form (if available).
- Verification all HUD Clinicians have completed the HUD manufacturer training, if required.
- Verification all HUD clinicians have completed the required CITI training course.

Via the IRB electronic submission system all IRB members will have access to all the above information submitted by the Physician.

5.2 Consent for Clinical Use of HUD

Informed consent is not required by FDA regulations when a HUD is used for an approved indication, unless the use represents a clinical investigation. However, the IRB may require written and signed informed consent when treating or diagnosing a patient with a HUD in certain cases.

When available and feasible, any FDA-approved patient labeling information prepared by the manufacturer must be provided and reviewed with the patient prior to use of the HUD. The plan for how and when this will be done must be included in the HUD application.

5.3 Initial IRB Review

The initial review of a HUD must be done at an IRB convened meeting. As part of its review the IRB must:

- Evaluate the risks described in the product labeling and ensure that the risks are minimized
- Ensure that risks are reasonable in relation to anticipated benefits of the proposed use of the device
- When appropriate, ensure that each prospective patient or their legally authorized representative are adequately informed about the HUD
- Where appropriate, the plan for use of the HUD adequately monitors the safety of subjects
- Verify that proposed use of HUD corresponds with the current labeling and does not exceed the scope of the FDA-approved indication, and
- Evaluate whether the Physician and his/her clinical team is qualified through training and expertise to use the device.

The IRB may approve the use of the HUD without any restrictions beyond the FDA-approved labeling or may impose more stringent criteria for the use of the HUD as deemed necessary to provide adequate patient protections.

The IRB will determine and provide written notification to the Physician regarding continuing review/renewal frequency (i.e., at least annually) and whether it may occur via expedited review. Once approved, use of the HUD is restricted to personnel listed on the HUD application unless modified by the Physician.

5.4 Renewal/Continuing Review

The IRB will conduct continuing review of the use of the HUD at intervals appropriate to the degree of risk, but no less than once a year. Continuing review may be performed via expedited review.

The Physician is responsible for submitting the HUD Continuing Review Form and required information to the IRB in sufficient time (at least 4 weeks prior to expiration) to ensure that re-approval is obtained prior to application expiration date.

He/she is required to provide the following HUD-specific information at the time of continuing review:

- Number of times the HUD has been used during past approval period and total times used since initial approval
- Any problems associated with its use
- Any unanticipated problems, including serious adverse events and deviations since the last review
- Any use outside of the FDA approved labeling or emergency use
- Any information provided to the sponsor or FDA concerning use at other sites or any annual reports to the FDA (if applicable), and
- Any Medical Device Reporting reports or IRB of Record reports of events that required prompt reporting.

5.5 Modifications

Modifications to the HUD or proposed changes to the clinical use of the device must be submitted to the WSU IRB for review and approval prior to using the modified device or implementing the change to the clinical use.

To request a change, the Physician must complete the modification request associated with the initial HUD application in the IRB electronic submission system and attach the following documents to the submission:

- Copy of the FDA's approval of the modification
- Copy of HDE holder's amendments to the HUD product labeling, clinical brochure, and/or other pertinent materials pertaining to the requested amendment, and
- Revised consent form (if applicable).

5.6 Prompt Reporting

Whenever the Physician becomes aware of information, from any source, that reasonably suggest that a HUD has or may have caused or contributed to the death or **serious** injury of a patient, the Physician must report such findings to the FDA, HDE Holder (i.e., manufacturer) and the IRB as soon as possible, but no later than 5 working days after the Physician first learns of the effect or problem.

Serious injury means an injury or illness that (1) is life-threatening, (2) results in permanent impairment of a bodily function or permanent damage to a body structure, or (3) necessitates medical or surgical intervention to preclude permanent impairment of a bodily function or permanent damage to a body structure (21 CFR 803.3).

Information concerning the event must be submitted to the IRB using the electronic submission systems' Incident Submission. External adverse device effects that meet

the definition of serious and unanticipated should also be submitted in accordance with the *Incidents or Reportable Problems Policy*.

The Physician responsible for use of the HUD must report any FDA actions regarding the HUD to the IRB within 15 working days of being notified.

5.7 Collection of Safety and Effectiveness Data when HUD is Used in Accordance with its Approved Indications

Collection of safety and effectiveness data to support a PMA application by the HDE-holder for the HDE-approved indication may occur under the HDE without the need to obtain an Investigational Device Exemption (IDE).

However, this activity is considered by the FDA to represent a clinical investigation (i.e., research) and, as with other FDA-regulated clinical investigations, IRB approval and informed consent are required (21 CFR Part 56).

The Physician must follow IRB's submission requirements (see Policy 21) for such cases. Also, since the activity is now considered research, authorization from the subject or LAR under the HIPAA Privacy Rule is required for protected health information to be used or disclosed. HIPAA authorization template language must be included in the consent form.

Even when the data will not be submitted to the FDA, the collection of safety and efficacy related to use of the HUD for its approved indication by the Physician/investigator for activities meeting the OHRP or FDA definition of human subject research must follow the additional IRB of Record submission and review requirements for those activities representing FDA-regulated studies.

Clinical investigation of a HUD for a different indication than the HDE-approved indication must be conducted in compliance with the IDE regulations at 21 CFR Part 812, subject to IRB approval (21 CFR Part 56), and in compliance with protection of human subjects, including informed consent and, if applicable, additional safeguards for children (21 CFR Part 50). If the device is a significant risk device, an FDA-approved IDE is required before starting the clinical investigation.

5.8 Off-Label Use of HUD

Off-label (i.e., use for a non-HDE approved indication) use of the HUD requires review and approval by the convened IRB on a case-by-case basis, except for emergency or compassionate use. IRB approval for the HDE-approved indication must also occur before the off-label is reviewed. If the off-label use is part of a clinical investigation, procedures should follow those described in the *Research Involving Medical Devices*

Policy, including securing an IDE.

5.9 Emergency Use of HUD

The HUD may be used off-label (i.e., a non-approved indication) or without prior IRB approval in an emergency situation. To do so, the Physician must understand and follow the *Emergency Use Policy* which includes obtaining concurrence of the IRB chair or designee, informed consent from the patient or the patient's legally authorized representative, independent assessment from an uninvolved physician and authorization from the HDE holder.

5.10 Compassionate Use of HUD

The FDA allows the use of a HUD in circumstances where the device is the only option available for a patient faced with a serious or life-threatening condition that does not meet the criteria of an emergency. A use is commonly referred to as "compassionate use." Unlike emergency use, prior FDA approval is required before compassionate use occurs.

As a first step, the Physician should seek the approval of the HDE holder and provide them with the following information: 1) description of the patient's condition and circumstances necessitating, 2) discussion of why alternative therapies are unsatisfactory, an identification of any deviations from the approved HUD labeling required to treat the patient and patient protection measures that will be followed. The HDE holder must then submit an IDE (HDE) supplement to the FDA for approval.

Once FDA approval is obtained, the Physician should submit an initial application per Section 5.3 of this policy along with documentation of FDA approval of the compassionate use for IRB review and approval.

6.0 Records

All records related to this process will be stored and maintained in accordance with any Wright State policy, federal regulations and sponsor requirements associated with the human subject research protocol under review.

7.0 References:

- 21 CFR 814 subpart H
- 21 CFR 803.30
- 21 CFR 814.124(a)
- 21 CFR 812.35
- Guidance for HDE Holders, IRBs, Clinical Investigators, and FDA Staff – HDE Exemption Regulation: Questions and Answers, July 8, 2010.