IRB Oversight of Humanitarian Use Devices

(What's an IRB to do?)

Robert 'Skip' Nelson, MD PhD

Deputy Director and Senior Pediatric Ethicist
Office of Pediatric Therapeutics, Office of the Commissioner
Food and Drug Administration, Silver Spring MD
<Robert.Nelson@fda.hhs.gov>

January 8, 2014

Objectives

- Note that a HUD can only be used following IRB approval (except in certain emergencies)
- Review the distinction between using a HUD in the course of medical practice and using a HUD in a clinical investigation
- Discuss IRB review procedures when a HUD is to be used in the course of medical practice
- Conclude with a summary of regulations governing HUD use in clinical investigations

HDE Guidance (Issued July 8, 2010)

- Guidance for HDE Holders, Institutional Review Boards (IRBs), Clinical Investigators, and FDA Staff - Humanitarian Device Exemption (HDE) Regulation: Questions and Answers.
  - Available at: http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm110194.htm (accessed December 30, 2013)

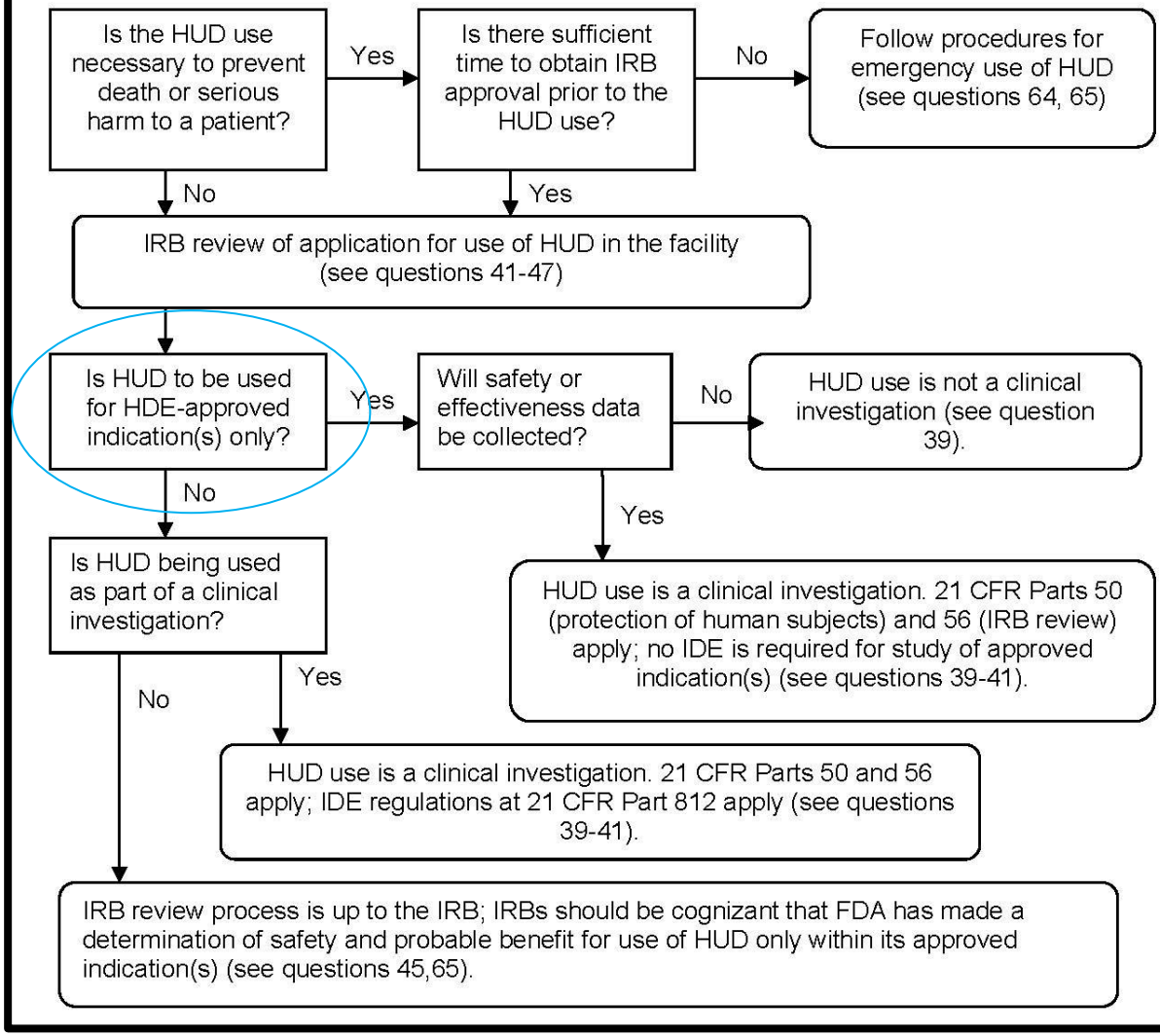
- *Caveat*: The 2012 Food and Drug Administration Safety and Innovation Act (FDASIA) amended section 520(m)(6) of the Federal Food, Drug, and Cosmetic Act. This guidance was developed and issued prior to the enactment of FDASIA, and certain sections of this guidance may no longer be current as a result of FDASIA. CDRH is working on an updated draft HDE guidance.

HUD and HDE

- A Humanitarian Use Device (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."
- A Humanitarian Device Exemption (HDE) indicates that the device is approved for marketing, but the approval is based on evidence of safety and probable benefit (rather than the "higher" standard of reasonable assurance of effectiveness).
- An HUD 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.

http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm110194.htm

Figure 1: Decision Tree for IRB Review of HUDs

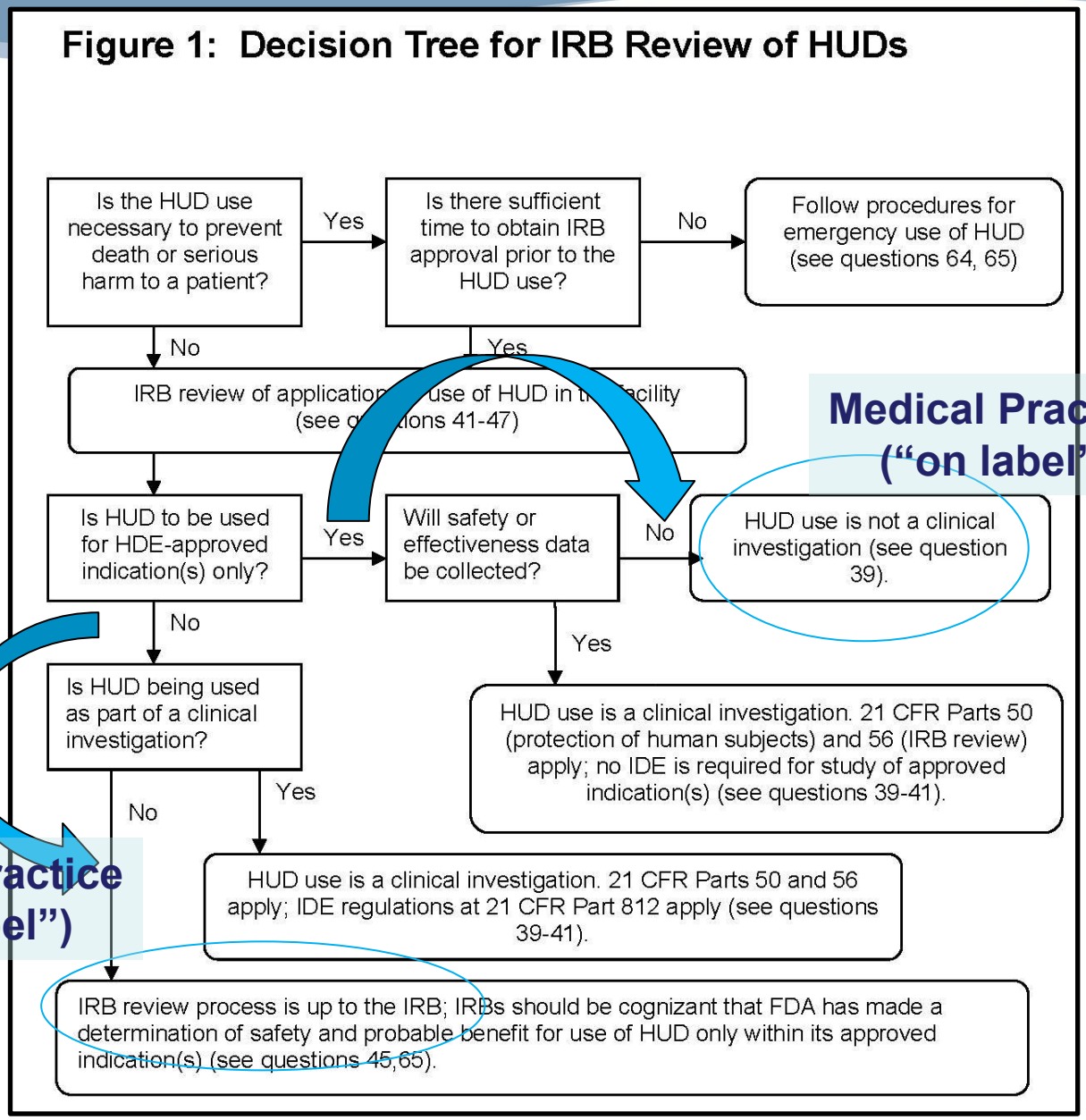


http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm110194.htm

What does it mean to "use" a HUD?

- A HUD can be used in two general ways.
  - *Medical Practice*: A HUD can be used according to its approved labeling and indication(s) to treat or diagnose patients. It can also be used "off label" as part of medical practice.
  - *Clinical Investigation*: A HUD can be used in a clinical investigation (i.e., collection of safety and effectiveness data). A HUD may be studied in a clinical investigation in accordance with its approved indication(s) or for a different indication.

Figure 1: Decision Tree for IRB Review of HUDs



Medical Practice ("on label")

Medical Practice ("off label")

http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm110194.htm

What's an IRB to do?

(when HUD is used in medical practice)

- Must an IRB review a protocol before approving HUD use?
  - **No.** Using a HUD to treat or diagnose patients (*not research*) does not require submission of a protocol to the IRB.
- Must an IRB monitor the number of HUD uses per year?
  - **No.** This is the responsibility of the HDE holder.
- Must an IRB audit the medical record of patients who received a HUD?
  - **No.**
- Should an IRB ask for justification of HUD charges?
  - **No.** FDA reviews the HDE holder's financial information.

http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm110194.htm

What's an IRB to do?
(when HUD is used in medical practice)

- Does an IRB function as HUD Data Monitoring Committee?
  - **No.** The IRB may ask the HDE holder for copies of the safety information submitted to FDA in the periodic reports.
- Do requirements for IRB review of a HUD change if an IRB applies 45 CFR 46 (i.e., DHHS regulations)?
  - **No.** The use of a HUD is not research; rather, it is use of a legally marketed device
- Must an IRB approve an informed consent document to be given to patients before they receive a HUD?
  - **No.** FDA does not require written informed consent from patients for the use of a HUD.

http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm110194.htm

What's an IRB to do?
(when HUD is used in medical practice)

- FDA recommends that an IRB follow the review criteria at 21 CFR 56.111 and elsewhere in Part 56 as much as possible.
- For example, an IRB should:
  - review the risks to patients that are found in the product labeling
  - ensure the risks are minimized, and
  - evaluate whether the risks are reasonable in relation to the proposed use of the device.
- Note: FDA has made a determination of safety and probable benefit for use of the HUD only within its approved indication(s).

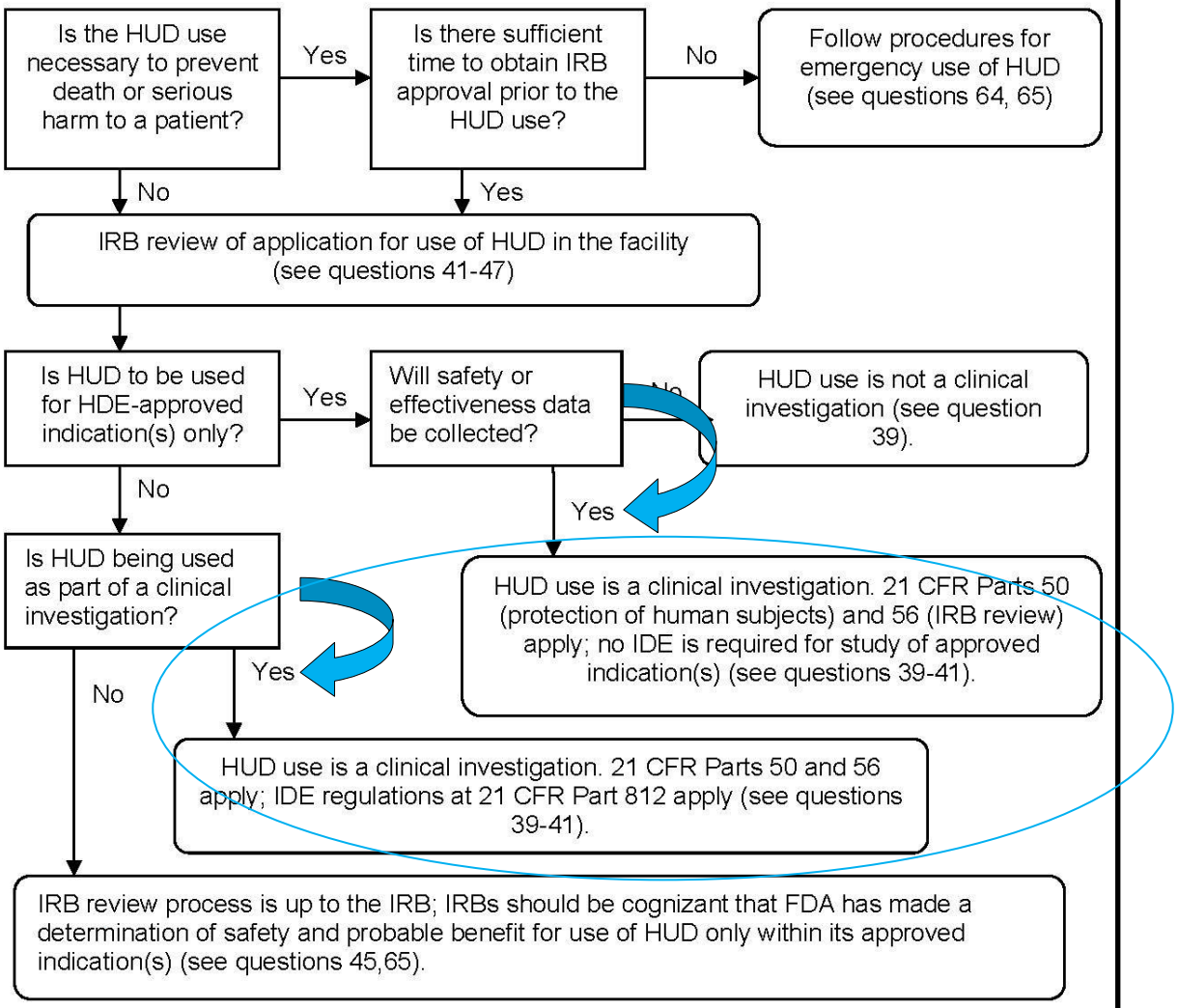
http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm110194.htm

What's an IRB to do?
(when HUD is used in medical practice)

- FDA recommends reviewing the following materials during initial review of HUD
  - copy of HDE approval order;
  - description of device;
  - product labeling;
  - patient information packet that may accompany HUD;
  - sample consent form for use of HUD, if required by IRB;
  - and summary of how physician proposes to use device, including
    - description of any screening procedures, HUD procedure, and any patient follow-up visits, tests or procedures.

http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm110194.htm

Figure 1: Decision Tree for IRB Review of HUDs



http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm110194.htm

Regulations Governing HUD Studies

- Prior to HDE approval, any studies using the device must be under IDE regulations (21 CFR Part 812) and must have IRB approval.
- Following HDE approval,
  - HDE holder may collect safety and effectiveness data in a clinical investigation for the HDE-approved indication(s) *without an IDE*.
  - Clinical investigation of HUD *for different indication* must be conducted in compliance with IDE regulations. To date, all HUDs have been significant risk devices requiring FDA-approved IDEs.
  - IRB approval (21 CFR Part 56) and protection of human subjects (21 CFR Part 50) are required as these are FDA-regulated clinical studies.

http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm110194.htm

HUD Studies Regulations in summary

- **IRB approval, informed consent, and additional safeguards for children (if applicable) are required for the investigational use of a HUD, whether the HUD is being studied for its HDE-approved indication(s) or for a different indication.**

http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm110194.htm

Thank you.