Data Safety Monitoring Board (DSMB)

What is it?

Why do we need it?

What is the role of the IRB?

DSMB: What is it?

- An independent committee
- Monitors data throughout the duration of the study to determine if continuation of the study is appropriate
  - Scientifically
  - Ethically
  - Stopping rules
  - May suggest modifications to the study
- Composition (typical)
  - Experts in the fields of medicine and science that are applicable to the study
  - Statistical experts
  - Lay representatives

DSMB: Why do we need it?

- NIH states that all clinical trials supported require some form of monitoring
- Risk and complexity are identified as the most important determinates of the degree and method of monitoring
  - Early studies (non-therapeutic, Phase I, Phase II)
    - It is permitted that the PI do the monitoring
  - All Phase III studies require a formal Data Safety Monitoring (DSM) plan
    - May include a DSMB
    - Low risk trials may not require a DSMB
- Factors that suggest a DSMB is needed:
  - Large study population
  - Multiple study sites
  - Toxic therapies, dangerous procedures, high expected rates of morbidity/mortality
  - High chance of early termination of the study

DSMB: What is the role of the IRB?

- The IRB is responsible for determining if a study needs formal ongoing monitoring of data to ensure that subjects will be protected.
- This responsibility stems from DHHS and FDA regulations stating a criterion for study approval be that
  - "when appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects" (45 CRF 46.111[a][6])
  - Belmont Report: minimization of risk
- The DSMB is not required to communicate with the IRB, HOWEVER the intent is that important information be reported to the IRB

Humanitarian Use Device and Humanitarian Device Exemption

- A Humanitarian Use Device (HUD) is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year.

Humanitarian Use Device and Humanitarian Device Exemption

- To obtain approval for an HUD, an humanitarian device exemption (HDE) application is submitted to FDA.
- An HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose.

Humanitarian Use Device and Humanitarian Device Exemption

- The application must contain sufficient information for the FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use.

Humanitarian Use Device and Humanitarian Device Exemption

- Additionally, the applicant 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.

Humanitarian Use Device and Humanitarian Device Exemption

- An approved HDE authorizes marketing of the HUD.
- An HUD may only be used in facilities that have established a local IRB to supervise clinical testing of devices, and after an IRB has approved the use of the device to treat or diagnose the specific disease.

Humanitarian Use Device and Humanitarian Device Exemption

- The labeling for an HUD must state that the device is an 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.

HDE: IRB Considerations

What are some of the differences between an HDE and IDE?

- FDA approval of an HDE authorizes an applicant to market a HUD in accordance with approved labeling and indications for use, subject to certain restrictions.
- If a HUD meets the HDE standards for approval, it is exempt from the requirement of establishing a reasonable assurance of effectiveness.

HDE: IRB Considerations

What are some of the differences between an HDE and IDE?

- A device being used under an approved **IDE** is a device that has not been cleared or approved by FDA for marketing but has been authorized for investigational use in an FDA-regulated clinical investigation.

HDE: IRB Considerations

What are some of the differences between an HDE and IDE?

- With this exemption, the investigational device can be shipped lawfully for the purposes of conducting clinical investigations of the device without complying with certain other requirements of the FD&C Act that would apply to devices in commercial distribution.

HDE: IRB Considerations

Should an IRB be concerned if there is a HUD that is approved under an HDE for one indication, while being studied or marketed for another indication that was not approved under an HDE?

- No. A HUD may be used in accordance with its approved indications for use while being studied under an IDE for a different indication.

HDE: IRB Considerations

Who is responsible for submitting materials to and obtaining approval from the IRB before the HUD is used at a facility?

- The HDE holder is responsible for ensuring that the HUD is administered only in facilities with properly constituted and functioning IRBs.

HDE: IRB Considerations

Who is responsible for submitting materials to and obtaining approval from the IRB before the HUD is used at a facility?

- The health care provider at such facilities should be responsible for obtaining IRB approval before use of the HUD, except in certain emergencies where prior IRB approval is not required.

HDE: IRB Considerations

To what extent should an IRB exercise oversight of clinician responsibilities in the use of a HUD?

- The IRB is not required to review and approve each individual use of a HUD. Rather, the IRB may use its discretion to determine how to approve use of a HUD.
- In reviewing the use of the HUD, IRBs should be cognizant that the FDA has made a determination of safety and probable benefit for use of the HUD only within its approved indication(s).

HDE: IRB Considerations

What types of review functions are IRBs responsible for with respect to HUDs?

- IRBs are responsible for initial as well as continuing review of the HUD. For initial review of a HUD, IRBs are required to perform their review at a convened meeting.
- For continuing review, IRBs may use the expedited review procedures.

HDE: IRB Considerations

Should an IRB be concerned if an HDE holder charges for a HUD?

- HDE holders may generally charge for the HUD that is used to treat or diagnose a patient. However, unless FDA determines that the HUD qualifies for an exception, HUDs cannot be sold for a price that exceeds the costs of research and development, fabrication, and distribution of the device.

HDE: IRB Considerations

Should an IRB be concerned if an HDE holder charges for a HUD?

- If a HUD is studied in a clinical investigation for a new indication, the sponsor of the clinical investigation cannot charge subjects or investigators a price higher than necessary to recover the costs of manufacture, research, development, and handling.
- Any costs for which a subject in a clinical investigation is responsible must, when appropriate, be provided in the informed consent document.

HDE: IRB Considerations

What information should be given to patients before they receive a HUD, and should patients consent to the HUD use?

- Neither the FD&C Act nor the regulations require informed consent from patients for the use of a HUD for its HDE-approved indication.
- An IRB may, however, choose to require informed consent that is consistent with the approved labeling when the IRB approves use of the HUD in a facility.

HDE: IRB Considerations

What information should be given to patients before they receive a HUD, and should patients consent to the HUD use?

- Most HDE holders develop patient information packets that generally contain a discussion of the potential risks and benefits of the HUD

HDE: IRB Considerations

What should IRBs tell physicians who want to study a HUD for a new indication?

- Physicians who want to study a HUD for a new indication must submit an IDE application to FDA if the device is a significant risk device

HDE: IRB Considerations

When can a HUD be used without prior IRB approval?

- If a physician in an emergency situation determines that IRB approval for the use of the HUD at the facility cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be used without prior IRB approval.

HDE: IRB Considerations

When can a HUD be used without prior IRB approval?

- The physician must, within 5 days after the emergency use of the device, provide written notification of the use to the IRB chair person. The written notification must include the identification of the patient involved, the date of the use, and the reason for the use.

HDE: IRB Considerations

After an IRB approves the use of the HUD at the facility, can a physician use a HUD outside its approved indication in an emergency or if the physician determines there is no alternative device for the patient's condition?

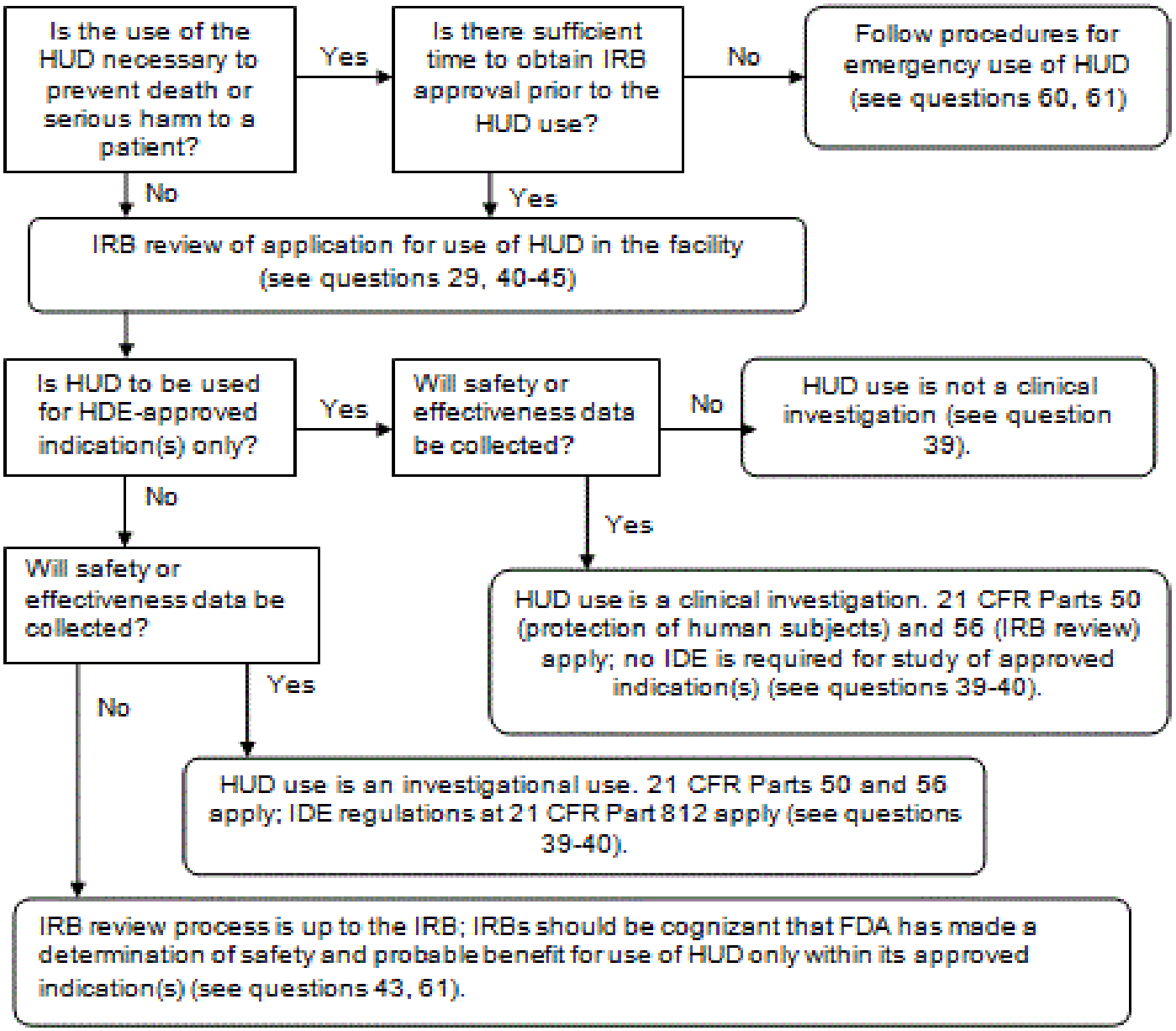
- The FDA has made a determination of safety and probable benefit for use of a HUD approved under an HDE only within its approved indication.

HDE: IRB Considerations

- If a physician wants to use a HUD outside its approved indication, FDA recommends that the physician obtain informed consent from the patient and ensure that reasonable patient protection measures are followed.

HDE: IRB Considerations

- The FDA recommends that the physician submit a follow-up report on the patient's condition to the HDE holder and first check with the IRB before such use to review any institutional policy. The extent of IRB oversight in these circumstances is up to the IRB.


Is the use of the HUD necessary to prevent death or serious harm to a patient?
Yes
Is there sufficient time to obtain IRB approval prior to the HUD use?
No
Follow procedures for emergency use of HUD (see questions 60, 61)
No
Yes
IRB review of application for use of HUD in the facility (see questions 29, 40-45)
Is HUD to be used for HDE-approved indication(s) only?
Yes
Will safety or effectiveness data be collected?
No
HUD use is not a clinical investigation (see question 39).
No
Yes
Will safety or effectiveness data be collected?
HUD use is a clinical investigation. 21 CFR Parts 50 (protection of human subjects) and 56 (IRB review) apply; no IDE is required for study of approved indication(s) (see questions 39-40).
No
Yes
HUD use is an investigational use. 21 CFR Parts 50 and 56 apply; IDE regulations at 21 CFR Part 812 apply (see questions 39-40).
IRB review process is up to the IRB; IRBs should be cognizant that FDA has made a determination of safety and probable benefit for use of HUD only within its approved indication(s) (see questions 43, 61).