An HUD may be administered a single time without prior approval by the IRB in an emergent situation in which a physician determines that approval from the IRB cannot be obtained in time to prevent serious harm or patient death.

The FDA recommends that the physician obtain informed consent from the patient and ensure that reasonable patient protection measures are followed, such as devising schedules to monitor the patient, taking into consideration the patient's specific needs and the limited information available about the risks and benefits of the device.

The FDA further 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.

In such an emergency situation, the physician shall, within 5 days after the use of the device, provide written notification to the IRB of such use.

Note: user facilities must submit reports to FDA, the IRB of record, and the manufacturer whenever a HUD may have caused or contributed to a death, and must submit reports to the manufacturer (or to FDA and the IRB of record if the manufacturer is unknown) whenever a HUD may have caused or contributed to a serious injury.

8.8 EMERGENCY USE AND EXPANDED ACCESS FOR MEDICAL DEVICES

An unapproved device usually may only be used on human subjects through an approved clinical study in which the subjects meet certain criteria and the device is only used in accordance with the approved protocol. Circumstances under which a health care provider may wish to use an unapproved device to save the life of a patient or to help a patient suffering from a serious disease or condition for which there no other alternative therapy exists. The use of an investigational device outside of a clinical trial for treatment of a patient is called "expanded access."

If enrollment in an existing clinical trial protocol is not possible (e.g., a patient is not eligible for any ongoing clinical trials, or there are no ongoing clinical trials to address the patient's condition), patients/physicians have the potential to receive expanded access to investigational devices under one of three alternative mechanisms:

- Emergency Use
- Compassionate Use (or Single Patient/Small Group Access)
- Treatment Use

A. Emergency Use

Emergency use is the use of an investigational device in an emergency situation. It is intended to provide patients and physicians with access to devices intended to treat life-threatening or serious diseases or conditions when there is no available alternative and no time to obtain FDA approval. Emergency use may apply even if the investigational device is being studied in a clinical trial under an IDE: if a physician needs to use the device in a manner inconsistent with the approved investigational plan; or a physician who is not part of the clinical study, wishes to use the device to treat a patient with a life-threatening or serious disease or condition. Emergency use of an investigational device may occur before an IDE is approved and when a device is not being studied under an IDE.

A physician may treat a patient with an unapproved device in an emergency situation if he/she concludes that:

a. The patient has a life-threatening condition that needs immediate treatment;

b. No generally acceptable alternative treatment for the condition exists; *and*

c. Because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

If all of the above criteria are met, an unapproved device may be used in an emergency situation without prior approval by FDA. FDA expects the physician to make the determination that the patient's circumstances meet the above criteria, to assess the potential for benefit from the use of the unapproved device, and to have substantial reason to believe that benefits will exist.

If a device is used in circumstances meeting the criteria listed above, the physician should follow as many of the patient protection procedures listed below as possible:

a. Informed consent from the patient or a legal representative;

b. Clearance from the Institution;

c. Concurrence of the IRB chair;

d. An independent assessment from an uninvolved physician; and

e. Authorization from the device manufacturer.

Prior approval from the FDA for shipment or emergency use of the investigational device is not required.

When the physician determines that the use of the unapproved device in the patient meets the criteria for emergency use and there is sufficient time to obtain IRB Chair review, the following is to be submitted via Cayuse IRB for concurrence of the emergency use:

a. Initial Application in Cayuse IRB: A description of the patient's disease, including recent medical history and previous treatments outlining the rationale for the use, an explanation of that there is no generally acceptable alternative treatment for the condition that exists and there is no time to use existing procedures to get an IDE for the use. The submission is also to include the method of administration, and duration of therapy, a description of the clinical procedures, laboratory tests, or other monitoring necessary to evaluate the effects of the device and minimize its risks. This summary information must support the criteria for emergency use above.

b. A copy of the written informed consent that will be used to obtain informed consent. The consent form must explain the purpose of the use of this device. The consent document must not include references to a research investigation, however, it must include an explanation of what data will be collected regarding the administration and the reporting requirements to the FDA and IDE sponsor (if applicable). If the physician is unable to obtain consent, the submission must include a justification for an exception and must meet the criteria for exception to obtaining informed consent.

c. Any relevant safety information from the device manufacturer or patient information materials.

d. Documentation of communication with the FDA, if applicable.

e. Documentation that the physician has access to the device or documentation of the decision from the supplier of the device that they will ship the product and authorize its use.

If the test article is a device with an FDA-approved IDE, the treating physician is responsible to notify the device sponsor of the emergency use.

The emergency use of the device should be reported to FDA by the IDE sponsor via a supplement within 5-working days from the time the sponsor learns of the use. The supplement submitted to the FDA should contain a summary of the following:

a. Conditions constituting the emergency

b. The patient protection measures that were followed such as:

- Informed consent from the patient or a legal representative;
- Clearance from the Institution;
- Concurrence of the IRB Chair or his/her designee;
- An independent assessment from an uninvolved physician; and
- Authorization from the IDE sponsor, if an approved IDE exists for the device.

c. Patient outcome information

If an FDA-approved IDE does not exist for the device, the information above should be submitted by the treating physician directly to the FDA.

B. Compassionate Use (or Single Patient/Small Group Access)

The compassionate use of an IDE provides a mechanism for patients with serious disease or condition, for which there is no alternative treatment available and who do not qualify for inclusion in a clinical investigation, access to an investigational device which the treating physician believes may provide a benefit in treating and/or diagnosing. It can also be used for devices that are not being studied in a clinical investigation (i.e., an IDE for the device does not exist). This provision is typically approved for individual patients but may be approved to treat a small group.

The criteria for compassionate use of an investigational device are:

- The patient has a life-threatening or serious disease or condition; and
- No generally acceptable alternative treatment for the condition exists.

FDA approval is required before compassionate use occurs. Physicians (if there is no current IDE for the device), or sponsors (who has submitted the IDE to conduct the clinical study for the device), are required to submit an IDE Supplement containing the following to the FDA when requesting a compassionate use of an investigational device:

a. A description of the patient's condition and the circumstances necessitating treatment;

b. A discussion of why alternatives therapies are unsatisfactory and why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition;

c. An identification of any deviations in the approved clinical protocol (if applicable) that may be needed in order to treat the patient

d. The patient protection measures that will be followed:
   - A draft of the informed consent document that will be used;
   - Concurrence of IRB chairperson;
   - Clearance from the Institution;
   - Independent assessment from an uninvolved physician; and
   - Authorization from the device manufacturer on the use of the device.

The above compassionate use criteria and procedures can also be applied when a physician wishes to treat a small group of patients. In this case, the physician should request access to the device through the IDE sponsor. The sponsor should submit an IDE supplement that includes the information identified above and indicates the number of patients to be treated. Such a supplement should include the protocol to be followed or identify deviations from the approved clinical protocol.

A monitoring schedule should be designed to meet the needs of the patients while recognizing the investigational nature of the device. Follow-up information on the use of the device should be submitted in an IDE supplement after all patients have been treated.

The treating physician is to submit the following documents to the IRB for review of the compassionate use:

a. Initial Application in Cayuse IRB: an outline of the rationale for the use, an explanation of why use of this device is preferable to the use of available therapeutic options, description of the patient's (or patients') disease, the method of administration of the device, and duration of therapy, description of the clinical procedures, laboratory tests, or other monitoring necessary to evaluate the effects of the device and minimize its risks.

b. A copy of the written consent form that will be used to obtained informed consent. The consent form must contain all the elements of consent per FDA regulations, and must explain the purpose of the use of this investigational device. The consent document must reference the investigation as a treatment and it must include an explanation of what data will be collected regarding the administration, to whom it will be shared and for what purpose(s), and the reporting requirements to the FDA and/or sponsor

c. The approval from the FDA of the compassionate use of the device.

d. Documentation of an independent assessment from an uninvolved physician.

e. A statement from the sponsor of the IDE that they will provide the device; including a description of what costs the patients will incur, if any, from the use of the device.

Once the review is submitted to the IRB, the Compassionate use IDE documents will be reviewed by the IRB Chair for concurrence.

C. Treatment Use

If data from a clinical trial suggests that an investigational device is effective, the trial may be expanded to include additional patients with life-threatening or serious diseases for whom no comparable alternatives are available. During the clinical trial, or prior to final action on the

marketing application, it may be appropriate to use the device in the treatment of patients not in the trial under the provisions of the Treatment IDE regulation (21 CFR 812.36).

The FDA would consider the use of an investigational device under a Treatment IDE if:

- The device is intended to treat or diagnose a serious or immediately life-threatening disease or condition;
- There is no comparable or satisfactory alternative device or other therapy available to treat or diagnose that stage of the disease or condition in the intended patient population;
- The device is under investigation in a controlled clinical trial for the same use under an approved IDE, or such clinical trials have been completed; and
- The sponsor of the investigation is pursuing marketing approval/clearance of the investigational device.

The use of an investigational device for Treatment Use requires an IDE application submitted to the FDA for approval.

If the IDE application for the treatment use of the device is approved by the FDA, the physician should submit the following documents to the IRB for review and approval by the IRB:

a. Initial Application in Cayuse IRB: the rationale for the use, including, as appropriate, either a list of the available regimens that ordinarily should be tried before using the investigational device or an explanation of why the use of the investigational device is preferable to the use of available marketed treatments; and a description of the clinical procedures, laboratory tests, or other monitoring necessary to evaluate the effects of the device and minimize its risks.

b. Information that is relevant to the safety and effectiveness of the device for the intended treatment use. Information from other IDE's may be incorporated by reference to support the treatment use.

c. A copy of the written consent form that will be used to obtained informed consent. The consent form must contain all the elements of consent per FDA regulations, and must explain the purpose of the use of this device, and the description of the data that will be collected to report safety and effectiveness data to the FDA and sponsor or collected in support of the device approval.

d. The approval from the FDA of the treatment use of the device.

e. A statement from the sponsor of the IDE that they will provide the device; including a description of what costs the patients will incur, if any, from the use of the device.

Once the review is submitted to the IRB, the Treatment IDE documents will be reviewed at a convened IRB meeting, following standard IRB procedures. All Treatment IDEs do not meet the criteria for expedited review and it must go to the full IRB for review. Since it involves the use of an investigational device, it does not qualify as minimal risk.

The sponsor of a Treatment IDE must submit progress reports on a semi-annual basis to the FDA until the filing of a marketing application. After filing of a marketing application,

progress reports must be submitted annually in accordance with applicable IDE regulations. The sponsor of a Treatment IDE is responsible for submitting all other reports required under 21 CFR 812.150; such as unanticipated adverse device effects and final reports. The reports are submitted as supplements to the original IDE application.

8.9 OFF-LABEL USE OF MARKETED DRUGS, BIOLOGICS, AND DEVICES

At the time that the FDA approves a new drug, biologic, or device for marketing, it also specifies the indications, patient groups, and formulation under which the drug, biologic, or device may be used. Any variance from these approved specifications constitutes “off-label” usage.

If physicians use a product for an indication not in the approved labeling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and on sound medical evidence, and to maintain records of the product's use and effects. Good medical practice and the best interests of the patient require that physicians use legally available drugs, biologics and devices according to their best knowledge and judgement. Use of a marketed product in this manner when the intent is the "practice of medicine" does not require the submission of an IND or IDE to the FDA or review by the IRB.

8.10 FDA CONTACTS

- For drug products: Drug Information Branch at (301) 796-3400; druginfo@fda.hhs.gov; Questions about whether a product is subject to IND regulations: call (301)796-3400
- For biological products: (301) 827-2000; Questions about whether a product is subject to IND regulations: call 301-827-2000
- For device products: visit the webpage: Division of Industry and Consumer Education (DICE); DICE@fda.hhs.gov
- For physicians seeking information on Expanded Access/ Emergency Use visit this FDA webpage.
- FDA Emergency Call Center, telephone: 866-300-4374 after 4:30 pm EST weekdays and all day on weekends.