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VA MEDICAL CENTER  
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MEDICAL CENTER POLICY 151-015  
September 1, 2007

## INVESTIGATIONAL DEVICES USED IN HUMAN STUDIES

1. **PURPOSE.** To ensure that all devices used in conjunction with investigational protocols involving human subjects are used only after the patient has signed the informed consent form specific for the investigational device to be used. An Investigational Device Exemption (IDE) number must be included, if applicable.
2. **POLICY.** It is the Medical Center's policy to adhere to all FDA and VHA regulations concerning Investigational Devices.
3. **DEFINITIONS.**
  - a. **Investigational Device.** An investigational device is a medical device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. As further stated, a device is any healthcare product that does not achieve its primary intended purpose by chemical action or by being metabolized.
  - b. **Investigational Device Exemption (IDE).** IDE means an investigational device exemption in accordance with 21 CFR 812.
  - c. **Significant Risk (SR) Device.** Significant risk device means an investigational device that:
    - (1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; or
    - (2) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; or
    - (3) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
    - (4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
  - d. **Non-Significant Risk (NSR) Device.** A non-significant risk device is an investigational device other than a SR device.
  - e. **Unexpected Adverse Device Effect.** An unexpected adverse device effect is any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan

or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects (21 CFR 812.3(s)).

f. **Emergency Use.** Emergency use is defined as the use of an investigational drug or biological product in a human subject who is in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain Institutional Review Board (IRB) approval.

g. **Humanitarian Use Device (HUD).** Humanitarian Use Device is a device intended to benefit patients by treating or diagnosing a disease that affects fewer than 4,000 individuals in the United States per year. A humanitarian device exemption application is not required to contain the results of scientifically valid 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 or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use. The labeling for an HUD must state that the device is a HUD and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated.

#### 4. **RESPONSIBILITIES:**

##### a. **Principal Investigators (PI)**

(1) The PI is responsible for ensuring that the research is conducted according to all regulatory guidelines and LSCDVAMC policies and procedures.

(2) The PI must obtain approval from the R&D Committee and IRB before initiating any research activities.

(3) The PI must indicate on the IRB application whether the research involves an investigational device. If so, the PI must indicate if there is an IDE for the research and provide documented assurance from the sponsor that the manufacture and formulation of the investigational or unlicensed test article conforms to federal regulations. Documentation of the IDE must be provided. If there is no IDE, the PI must provide a rationale why it is not required.

(4) The PI proposing the device research will be required to provide a plan – to be evaluated by the R&D Committee and the IRB - that includes storage, security, and dispensing of the device.

(5) The PI must obtain approval from the Environment of Care (EoC) Committee for any electrically line-operated devices, which have leads or electrodes and that will come in contact with human subjects.

(6) The PI is responsible for the investigational device accountability that includes storage, security, dispensing, administration, return, disposition, and records of accountability.

(7) All devices received for a study must be stored in a locked environment under secure control with limited access. The area must be within an area of PI's control. Proper instructions on the use of the device must be provided to the subjects. A log must be kept regarding the receipt, use, and/or dispensing of the device and the disposition of remaining devices at the conclusion of the investigation (See the attached document at the end of this policy "Example of Investigational Device Control Log.").

(8) The PI will maintain the following:

- (a) Current curriculum vitae (CV)
- (b) Protocol of the study
- (c) Records of animal study reports
- (d) Records of receipt and disposition of devices
- (e) List of any co-investigators with their curriculum vitae
- (f) Certification that all physicians, dentists, and/or nurses responsible in the study have appropriate valid licenses for the duration of the investigation
- (g) Case histories with particular documentation on evidence of effects. Emphasis is on safety and possible untoward happenings.
- (h) R&D, IRB and Research Safety Committee letters of approval
- (i) Device training
- (j) Other documents as outlined in the Human Subject Protection Program Standard Operating Procedures.

(9) If a device is considered NSR by the PI or sponsor, but after review the IRB determines the device to have SR, upon receipt of written notice the PI is responsible for notifying the sponsor of the IRB's determination. The PI must provide the IRB with confirmation of this action.

(10) If the PI is storing the devices, he/she must maintain a log indicating the identification/serial number of the device, name of subject, date dispensed, by whom it was dispensed, and amount remaining. The PI will document in a Computerized

Patient Record System (CPRS) progress note that he/she provided education on its use to the subject.

(11) The PI must and other research personnel may use investigational devices after they have been given and have demonstrated an understanding regarding functional information about the device. This training must be documented and the PI must maintain records of this training.

(12) The PI shall report all unanticipated problems involving risk to subjects or others to the IRB.

(13) The PI will submit to the sponsor and to the IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.

(14) Following completion of the study the termination procedure for investigational devices must be applied, the log must be completed regarding the receipt, use and/or dispensing of the device and the disposition of remaining devices at the conclusion of the investigation.

(15) If, after use, the PI keeps the devices, he/she must maintain a log regarding the receipt, use and/or re-dispensing of the device and the disposition of remaining devices at the conclusion of the investigation.

(16) The PI will submit to the sponsor and to the IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.

(17) When a PI files an IDE, the PI is considered the sponsor and as such is accountable for all of the FDA regulatory responsibilities and reporting obligations of both the PI and the sponsor, as described in the FDA regulations (see Sponsor Responsibilities below).

#### b. IRB

(1) The IRB will review the research in accordance with the following requirements and the same criteria it would use in considering approval of any research involving an FDA-regulated product (21 CFR 56.111).

(2) The IRB will review the application and determine whether there is an IDE and if so, whether there is appropriate supporting documentation. If there is no IDE, the IRB will determine whether it is exempt under IDE regulations.

(3) The IRB will review the protocol and determine if the device represents SR or NSR and report the findings to the PI in writing. The IRB will consider the risks and benefits of the medical device compared to the risks and benefits of alternative

devices or procedures. NSR device studies do not require submission of an IDE application but must be conducted in accordance with the abbreviated requirements of IDE regulations. If the study that has been submitted as NSR is considered SR, the PI must obtain an IDE as recommended by the IRB.

(4) The IRB will not review protocols involving SR devices under expedited review.

(5) The IRB will document in the minutes and provide written documentation to the PI of the rationale for determining whether a device is classified as NSR/SR.

#### **c. R&D Committee Coordinator(s)**

(1) The R&D Committee Coordinator(s) will forward the R&D Committee and IRB approval letters and all approval documents to the PI.

**d. Sponsors:** The sponsor of a clinical investigation initiates and holds the IDE for a clinical investigation, but may not actually conduct the investigation. Although the sponsor is usually a pharmaceutical, biotech, or medical device company, an individual or group of individuals can also be considered a sponsor for an investigation. An investigator is referred to as the sponsor-investigator when the individual investigator is also the initiator of the clinical investigation. The responsibilities of sponsors and sponsor-investigators include the following:

- (1) Maintaining the IDE
- (2) Obtaining qualified investigators and monitors
- (3) Providing necessary information and training for investigators
- (4) Monitoring the investigation
- (5) Controlling the investigational product
- (6) Reporting significant adverse events to FDA/investigators
- (7) Maintaining and retaining accurate records

#### **5. PROCEDURES:**

a. The following procedures apply to investigational devices that are not radioactive. See below for guidance for radioactive materials that require approval by the Radiation Safety Committee. The Radiation Safety Committee will define specific documentation, storage and accountability procedures.

(1) Any device used in conjunction with an investigational protocol shall be kept in a locked and secured area.

(2) Access to devices shall be limited to personnel designated by the PI.

(3) A device inventory log will be kept on all investigational studies. The log will include only information concerning the equipment that is investigational or shipped specifically for the study.

(4) The log will include the following information:

- (a) Study name
- (b) IRB number
- (c) Sponsor name or funding agency
- (d) PI name
- (e) Type of device
- (f) Device model number
- (g) Device serial number
- (h) Lot number (if applicable)
- (i) Person receiving the device from storage (if applicable)
- (j) Date device was received
- (k) Date device was implanted or used
- (l) Patient name
- (m) Patient medical record number
- (n) Date device returned to sponsor or disposition (If product is returned to the sponsor or destroyed, documentation of why, when and persons involved.)

(5) These records shall be maintained in the project files or in the project's regulatory binder, and for the same period of time as indicated by the sponsor.

b. Emergency Use. FDA defines emergency use as the use of an investigational device in a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval. If all conditions described in 21 CFR 56.102(d) exist, then the emergency exemption from prospective IRB approval found at 21 CFR 56.104(c) may be utilized. Informed consent is required unless the conditions for exemption are met. The IRB must be notified within 5 working days when an emergency exemption is used. Any subsequent use of the test article at the institution is subject to IRB review.

The prospective PI is strongly encouraged to notify the COS/WP or designee in the event that he/she plans to use the emergency exemption from prospective IRB approval. This administrative notification is not required in the event that time does not permit.

If the PI notified the IRB prior to the emergency use of an investigational test article, the circumstances will be reviewed to determine that it meets FDA regulations and the PI will be advised accordingly. All after-the-fact reports to the IRB of emergency use will be reviewed by the IRB to determine the circumstances for compliance with FDA regulations.

### c. Ionizing Radiation Sources

(1) **Radioactive Materials in a Radiation Delivery Device:** The PI must obtain approval from the LSCDVAMC Radiation Safety Committee for any research protocol involving a radioactive source in a radiation delivery device. The approval process includes designation of an individual with the appropriate training to be the Authorized Physician User. The Authorized Physician User, who may not be the PI, is responsible for implementing all radiation safety instructions imposed by the Radiation Safety Committee.

(2) **Radiation Generating Equipment:** The PI must obtain approval from the LSCDVAMC Radiation Safety Committee for any research protocol involving an ionizing radiation generator intended to irradiate subjects. The approval process includes designation of an individual with the appropriate training to be the Authorized Physician User. The Authorized Physician User, who may not be the PI, is responsible for implementing all radiation safety instructions imposed by the Radiation Safety Committee. The Radiation Safety Officer must be notified at least 15 days in advance of the transfer, relocation or disposal of any ionizing radiation generator. New and transferred ionizing radiation generators must be tested and accepted by a Certified Radiation Expert in Radiology or Radiation Oncology, as appropriate, prior to first use on a human subject.

6. **REFERENCES.** VHA Handbook 1200.5; Human Research Protection Program Standard Operating Procedures, 21 CFR Parts 50, 56, 803, 812 and 814; FDA Information Sheet Guidance for IRB's, Clinical Investigators, and Sponsors (2006)

7. **RESCISSION.** Medical Center Policy 151-015 dated September 1, 2004 was rescinded. The review date for this policy is September 1, 2007.

8. **FOLLOW-UP RESPONSIBILITY.** Associate Chief of Staff for Research.

WILLIAM D. MONTAGUE  
Medical Center Director

Attachment

