Human Research Protection Program SOP # 23 Revised March 3, 2015

EMERGENCY USE OF A TEST ARTICLE or HUMANITARIAN USE DEVICE (HUD)

1. POLICY

The Birmingham VA Medical Center (BVAMC) Human Research Protection Program (HRPP) is committed to complying with all federal requirements applicable to emergency use of a test article. These include VHA Handbook 1200.5 Requirements for the Protection of Human Subjects in Research and FDA regulations in 21 CFR 50, 312, and 812 that mandates the direction and procedures related to the appropriate handling of emergency use of a test article. This BVAMC HRPP standard operating procedure (SOP) is the written policy and procedure regarding emergency use of a test article and the use of a HUD.

Within VA, emergency use of a test article is not considered to be research. Therefore, the patient is not a research subject, the emergency care cannot be claimed as research, and the outcome of such care cannot be included in any report of research activity subject to 38 CFR Part 16. FDA regulations at 21 CFR 56.104(c) permits the emergency use of a test article without IRB review. Emergency use is defined as use of a test article on 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 (21 CFR 56.102(d)). Ordinarily, the investigator must obtain the informed consent of the subject for such an emergency use, except as described below.

“Planned emergency research” differs from “emergency use” situations because planned emergency use involves IRB approval of a research study before the emergency arises (21 CFR 50.24). Planned emergency research is not permitted at the BVAMC.

Although individuals receiving a test article under the FDA regulations describing emergency use are considered human subjects under FDA regulations for purposes of this policy, they are not human subjects under the Common Rule because there is no prior IRB review and approval. However, under FDA regulations, the emergency use of a test article, other than a medical device, is a clinical investigation, the patient is a subject, and the FDA may require data from an emergency use to be reported in a marketing application. Therefore, the activity cannot be claimed as research under the Common Rule and the outcomes of such care cannot be included in any report of a research activity that is subject to the Common Rule.

2. RESPONSIBILITIES

BVAMC Director is responsible for assuring that all VHA Directives, FDA, federal, state and local regulations are followed by the BVAMC HRPP, including mandates for emergency use of test articles and HUD’s.
Chief of Staff, Research and Development (ACOS/R&D) is responsible for assuring that policies and procedures are implemented, operational and complied with, including those SOPs regarding emergency use of a test article and HUD’s.

R&D Committee is responsible for final approval or disapproval of IRB reviewed and approved studies and for oversight of all research activities conducted at the BVAMC.

The Institutional Review Board (IRB) is responsible for reviewing all research activities involving human subjects for compliance with all applicable federal, VA, and FDA regulations, policies, and guidelines for the protection of human subjects, including HUD’s.

Chief of Pharmacy Service is responsible for assuring the receipt, storage, security, dispensing and disposition of unused stocks of investigational drugs in Pharmacy for Research, and following guidelines outlined in VHA Handbook 1108.04, Investigational Drugs and Supplies and all applicable federal, FDA and VA policies concerning investigational drugs/devices.

Research Pharmacist is responsible for following all policies and procedures outlining the receipt, storage, custody, security, dispensing and disposition of unused stocks of investigational drugs and devices in Pharmacy for Research.

The Principal Investigator (PI) is responsible for adhering to this HRPP SOP and SOP #13, Investigator Responsibility, in regards to protecting the rights, safety and welfare of participants under the investigators care with studies involving the a HUD. The PI is responsible for assuring that investigational drugs are administered to study participants under their supervision only and not administered to/or by unauthorized individuals.

Clinicians are responsible to follow regulations and procedures as outlined in this SOP if considering use of an investigation drug or device under the emergency use of a test article. The clinician is responsible for retaining records for a period of two years following the date a marketing application is approved for the drug if utilized with the emergency test article regulations. If no application is to be filed, or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified. The PI is responsible for all required FDA and any sponsor reports.

3. DEFINITIONS

See HRPP SOP #24: HRPP Definitions

4. PROCEDURES

a. Procedures for Emergency use of test articles- All clinicians who are considering use of an investigational drug or device under the emergency use of a test article regulations are strongly encouraged to prospectively notify the Chief of Staff (COS), the Chair of the IRB, or the ACOS/R&D to review the criteria for both emergency use and informed
consent requirements and discuss whether the clinical circumstance is applicable for these regulations. Initial communication within the facility may be telephonic to expedite patient care. Note this notification does not constitute IRB approval. If the use involves an investigational drug, the prescribing clinician must contact the Research Pharmacy to make arrangements for receipt, storage, dispensing, and accountability.

1) **Obtaining an IND**

   a) **Investigational Drugs or Biologies:**
   Emergency use of an investigational drug or biologic requires an IND (Investigational New Drug Application). The clinician must obtain an IND number from the manufacturer, if possible. If the manufacturer elects not to name the clinician on the IND, the clinician must then contact the FDA directly for an IND or obtain evidence of an IND Exemption.

   b) **Investigational Devices:**
   Emergency use of an investigational device requires an IDE (Investigational Device Exemption). Therefore, the clinician must contact the manufacturer to determine if the product can be made available for use under the company's IDE. If an IDE does not exist, the FDA expects the clinician to determine the following:

   - whether the criteria for emergency use have been met;
   - assess the potential for benefits from the unapproved use of the device and to have substantial reason to believe that benefits exist; and
   - assure the decision of the clinician that an "emergency" exists is not based solely on the expectation that IDE approval procedures may require more time than is available.

   If an investigational device is being used, the clinician is responsible for assuring that the device sponsor/manufacturer notifies the FDA immediately after an unapproved device is shipped for emergency use.

2) **Obtaining informed consent:**

   a) Even under emergency use of a test article, no patient may receive an investigational drug, biologic, or device without obtaining informed consent from the patient or the patient's legally authorized representative.

   b) Under FDA regulations, in order to use a test article in a life threatening situation, informed consent is not required because all of the following are true: the treating clinician and an independent physician who is not otherwise participating in the emergency use of a test article certify in writing all four of the following specific conditions:

   (1) The patient is confronted by a life-threatening situation, necessitating the use of the test article;
(2) Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the patient;
(3) Time is not sufficient to obtain consent from the patient’s legally authorized representative; and
(4) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the patient’s life.

3) Reporting Requirements:

a) The above written certification must be submitted to the IRB and COS within five working days after the emergency use of the test article. This reporting must not be construed as an approval for the emergency use by the IRB.

b) If time is not sufficient to obtain the independent physician determination before use of the test article, the actions of the treating clinician must be reviewed and evaluated in writing by an independent physician within 5 working days after the use of the test article.

   (1) The written evaluation must include whether each of these four conditions were met and submitted to the IRB and COS within 5 working days after the use of the test article.

c) A copy of the report must also be sent to the Pharmacy and Therapeutics Committees if the use involves an investigational drug. The report must include at a minimum:

   (1) Name of investigational drug, biologic, or device
   (2) Condition of use (ex. administration schedule and dosage, device implantation)
   (3) Date and name of individual contacted if prospective notification made with COS, IRB Chair, or ACOS/R&D
   (4) Patient’s diagnosis and outcome if known
   (5) Any adverse events or unanticipated problems occurring during or following test article administration
   (6) Likelihood of needing to use the test article again
   (7) Copy of the signed and dated subject informed consent form and progress note, or
   (8) Copy of the clinician’s progress note documenting exception to informed consent and
   (9) Copy of progress note written by an independent physician whether the conditions of exception to informed consent were met.

b. Procedures for Humanitarian Use Device (HUD) use: Informed consent is not required when treating or diagnosing a patient under a Humanitarian Device Exemption (HDE), but prospective informed consent should be obtained when feasible. Patient labeling information may also provide information about the potential risks and benefits of the HUD and informs patients about the humanitarian use of device and that effectiveness for the labeled indication has not been demonstrated in previous clinical trials.
1) **IRB and R&D Committee approval:**
   a) After the Humanitarian Device Exemption (HDE) has been granted FDA approval, IRB and R&D Committee approval must also be obtained prior to its use.
   b) Investigators must submit an application to the IRB. This application must also contain a copy of the HDE application submitted to the FDA, documentation of FDA approval, any consent document that may be used, and the patient labeling information.
   c) Initial IRB approval must be performed at a convened meeting of the Board. The IRB may approve use of the HUD without restrictions or may require review on a case-by-case basis. Applications to the IRB should describe the approximate number of the patients the investigator anticipates will be treated or diagnosed with the device.
   d) Continuing reviews for Humanitarian Use Devices can be expedited by the IRB Chair in any case unless there is a change in the device. If there is a change in the device, a full board review will be required.
   e) All unanticipated problems and adverse events involving the use of a HUD should be submitted to the IRB in accordance with policies and procedures involving the use of investigational devices under an IDE application.

2) **Reporting Requirements:**
   a) A written report from the investigator must be received in the IRB office within 5 days after the HUD has been administered.
   b) A copy of the report must also be sent to the Pharmacy and Therapeutics Committees if the use involves an investigational drug. The report must include at a minimum:
      
      (1) Name of investigational drug, biologic, or device  
      (2) Condition of use (ex. administration schedule and dosage, device implantation)  
      (3) Date and name of individual contacted if prospective notification made with Chief of Staff, IRB Chair, or ACOS/R&D  
      (4) Subject’s diagnosis and outcome if known  
      (5) Any adverse events or unanticipated problems occurring during or following HUD administration  
      (6) Likelihood of needing to use the HUD again  
      (7) Copy of the signed and dated subject informed consent form and progress note, or  
      (8) Copy of the investigator’s progress note documenting exception to informed consent and  
      (9) Copy of progress note written by an independent physician whether the conditions of exception to informed consent were met.

   e) The IRB Chair or designated IRB member is expected to assess whether or not the conditions for the use have been met and document the determination. This is
placed in the IRB files with a copy sent to the investigator. The IRB Administrator is responsible for maintaining this documentation in IRB records.

3) **Off-Label Use of Humanitarian Use Device**- Prior FDA approval for an emergency use of a HUD is recommended. If this is not feasible, FDA recommends that the procedures in the Expanded Access of Unapproved Devices be used as guidance.

4) **Future Research Designed to Obtain Marketing Approval**- If the holder of HDE develops a research protocol designed to collect safety and effectiveness data to support marketing of the device, the investigational study must receive prior IRB review and approval. While an Investigational Device Exemption (IDE) is not required if the device is used within the FDA approved HUD labeling, IDE regulations must be followed and consent must be obtained from prospective participants in accordance with the IRB approved application.

c. **Required Documentation to go to Research Pharmacy**
   1) Investigational drugs/devices and HUD’s must be dispensed by the Research Pharmacy.

   2) If the emergency use of a test article or HUD involves an investigational drug/device, the following must be given to the Research Pharmacy prior to dispensing the initial dose:

   a) Signed and dated informed consent form, (HUD applicable) or
   b) Progress note by the prescribing physician documenting exception to informed consent requirements (HUD applicable)
   c) Order/Prescription for the investigational drug/device/HUD
   d) VA Form 10-9012 (HUD applicable)
   e) Protocol (HUD applicable and use involves a protocol that is pending IRB submission or review)

**REFERENCES**

- HRPP SOP # 13, Investigator Responsibility
- HRPP SOP # 18, Allegations of Noncompliance
- MCM 119-20 Medication Management Policy
- MCM 119-21 Investigational Drugs
- VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research
- VHA Handbook 1108.4 Investigational Drugs and Supplies
- Title 21 CFR 812.3
- Title 21 CFR 50.25, CFR 56.102 (d) and CFR 56.104 (c)
5. ATTACHMENTS
   None

6. RESCISSIONS

7. REVIEW DATE
   January 1, 2021

Louis Dell’Italia, MD
ACOS, Research and Development