Procedure

Subject: Procedure for the Emergency Use of FDA Regulated Products

Procedure:
This procedure outlines the process for the emergency use of investigational drugs, agents, biologics, or devices.

I. Investigator’s Responsibilities.
   A. Requirements of the emergency use of investigational drugs, agents, or biologics.
      1. The emergency use of an investigational drug, agent, or biologic requires an IND. The Investigator must:
         (a) Contact the manufacturer of the drug, agent, or biologic first to determine if the test article can be made available for the emergency use under the manufacturer’s IND or IDE; or
         (b) The need for an investigational drug, agent, or biologic may arise in an emergency situation that does not allow time for submission of an IND. The FDA may authorize shipment of the test article in advance of the IND submission. Requests for such authorization must be made by the Investigator to the appropriate department at the FDA (See attached contact list).
      2. Prior verbal notification to the IRB of an emergency use followed by the submission of a letter from the Investigator which states the following:
         (a) The subject is in an immediate serious or life-threatening condition that needs immediate treatment;
         (b) No generally acceptable alternative for treating the subject is available; and
         (c) Because of the immediate need to use the drug, agent, or biologic, there is no time to obtain full IRB approval for the use; and
         (d) The activity is not a systematic investigation designed to develop or contribute to generalizable knowledge.
      3. Even for an emergency use, the Investigator is required to obtain informed consent of the subject or the subject’s legally authorized representative as for any other research in accordance with FDA regulations 21 CFR 50.20, 50.25, and 50.27 unless both the Investigator and a physician who is not otherwise participating in the clinical investigation certify in writing the following:
         (a) The subject is confronted by a life-threatening situation necessitating the use of the investigational drug, agent, or biologic;
         (b) Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
         (c) Time is not sufficient to obtain consent from the subject’s legal representative; and
         (d) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject’s life.
      4. If, in the Investigator’s opinion, immediate use of the test article is required to preserve the subject’s life, and if time is not sufficient to obtain an independent physician’s determination that the four conditions listed above apply, the
Investigator should make the determination and, within 5 working days after the use, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

B. After emergency use procedures for investigational drugs, agents, or biologics.
   1. The Investigator is required to submit a written follow-up report to the IRB within five (5) days of the emergency use of an investigational drug, device, or biologic. This report should include:
      (a) Name of the investigational drug, agent, or biologic;
      (b) Copy of the informed consent document;
      (c) Conditions under which the investigational drug, agent, or biologic was administered;
      (d) Date and time administered;
      (e) Subject protection measures;
      (f) Any adverse events or unanticipated problems to recipient or others; and
      (g) Outcomes, if known.
   2. Evaluate the likelihood of a similar need for the drug, agent, or biologic and if future use is likely, immediately initiate efforts to obtain IRB approval and an FDA approved IND for the drug, agent, or biologic’s subsequent use.

C. Requirements for emergency use of investigational (unapproved) medical devices.
   1. The Investigator is responsible for justifying to the FDA that an emergency actually existed. To be considered an emergency the following criteria must be met:
      (a) The subject is in a life-threatening condition that needs immediate treatment;
      (b) No generally acceptable alternative for treating the subject is available; and
      (c) Due to the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use; and
      (d) The activity is not a systematic investigation designed to develop or contribute to generalizable knowledge.
   2. The FDA expects the Investigator to determine the following:
      (a) Whether the criteria for emergency use have been met;
      (b) To assess the potential for benefits from the unapproved use of the device, and to have substantial reason to believe that benefits will exist; and
      (c) Assure that the decision of the Investigator that an “emergency” exists is not based solely on the expectation that IDE approval procedures may require more time than is available.
   3. The Investigator must assure that the device developer notifies the FDA immediately after an unapproved device is shipped for an emergency use. An unapproved device may not be shipped in anticipation of an emergency.
   4. The Investigator is expected to follow as many subject protection procedures as possible. These include:
      (a) Obtaining a written independent assessment by an uninvolved physician;
      (b) Obtaining informed consent from the subject or the subject’s legally authorized representative;
      (c) Notifying the IRB prior to the emergency use of the device who will notify institutional officials as applicable; and
      (d) Obtaining authorization from the IDE holder, if an approved IDE for the device exists.
   5. The Investigator is required to obtain informed consent of the subject or the subject’s legally authorized representative as for any other research in accordance with FDA regulations 21 CFR 50.20, 50.25, and 50.27 unless both the Investigator and a physician who is not otherwise participating in the clinical investigation certify in writing the following:
The subject is confronted by a life-threatening situation necessitating the use of the investigational (unapproved) medical device.

Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;

Time is not sufficient to obtain consent from the subject's legal representative; and

No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

6. If, in the Investigator’s opinion, immediate use of the test article is required to preserve the subject’s life, and if time is not sufficient to obtain an independent physician's determination that the four conditions listed above apply, the Investigator should make the determination and, within 5 working days after the use, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

D. After emergency use procedures for investigational (unapproved) medical devices.

1. The Investigator is required to submit a written follow-up report to the IRB within five (5) days of the emergency use of an investigational (unapproved) medical device. This report should include:
   (a) Name of the investigational device;
   (b) Copy of the informed consent document;
   (c) Conditions under which the investigational device was utilized;
   (d) Date and time utilized;
   (e) Subject protection measures;
   (f) Any adverse device effects, adverse events or unanticipated problems to recipient or others; and
   (g) Outcomes, if known.

2. The Investigator is to evaluate the likelihood of a similar need for the device occurring again, and if future use is likely, immediately initiate efforts to obtain IRB approval and an approved IDE for the device’s subsequent use.

3. If an IDE for the use does exist, the Investigator is to notify the sponsor of the emergency use, or if an IDE does not exist, the Investigator is to notify the FDA of the emergency use and provide the FDA with a written summary of conditions constituting the emergency, subject protection measures, and results.

E. Requirements for expanded access compassionate use for unapproved medical devices.

1. The Investigator is responsible for justifying that the individual or small group of individuals have a serious condition for which there is no alternative to the use of the device.

2. FDA approval must be sought prior to any use by the holder of the IDE. The IDE holder must send to the FDA an IDE supplement outlining:
   (a) An explanation of the circumstances constituting the need for the device;
   (b) The reasons alternatives are not acceptable;
   (c) Deviations from any current protocol, if applicable; and
   (d) Patient protection measures.

3. Patient protection measures include:
   (a) An independent assessment by an uninvolved doctor;
   (b) IRB Chair or his/her designee's acknowledgement of the use; and
   (c) Informed consent.

II. IRB Committee Responsibilities.

A. The emergency use of FDA regulated products requires the involvement of an IRB Chair or his/her designee.

B. The IRB Chair or his/her designee will be promptly notified of the Investigator’s intent for emergency use of an investigational drug, agent, biologic, or device.

C. The IRB Chair or his/her designee will evaluate the Investigator’s notification and guide the Investigator in adherence to the FDA regulations and institutional policies and
procedures, and to ensure that the use is not a systematic investigation designed to contribute to generalizable knowledge. The IRB Chair or his/her designee may request:
1. An authorization from the sponsor or manufacturer to allow the use by the Investigator for the test article;
2. An approved IND/IDE or a letter explaining exemption from the FDA;
3. An adequate description of the situation regarding the use of the test article with an independent physician’s certification, if applicable;
4. The informed consent document or the certification for the exception from obtaining informed consent; and
5. Any other materials that may aid in the evaluation of the request.

D. The full Committee will be notified of the emergency use of an FDA regulated product via the “FYI” section of the applicable IRB Committee Agenda.
E. The IRB Chair or his/her designee reviews the five (5) day follow-up report submitted by the Investigator to determine that the circumstances met the FDA regulations and was not a systematic investigation designed to develop or contribute to generalizable knowledge. If the use did not comply with these requirements, the IRB Chair will handle the matter as non-compliance.

III. Regulatory Compliance Analyst (RCA) Responsibilities.
A. It is the responsibility of the RCA to facilitate any inquiries from Investigators regarding the emergency use of the FDA regulated product.
B. The RCA will contact an IRB Chair or his/her designee to inform him/her of the Investigator’s notification of emergency use.
C. The RCA will promptly notify the HRPP Director of an Investigator’s notification for emergency use of an FDA regulated product.
D. The RCA will assist the Investigator in providing the appropriate documentation prior to the emergency use, if possible, and follow-up with the Investigator if an adequate written report is not received within 5 days following the emergency use.
E. The RCA will update the HRPP database accordingly.

IV. VUMC Investigational Drug Services (IDS) Pharmacy Responsibilities.
A. Any investigational drug, agent, or biologic utilized in an emergency use setting must be dispensed through the IDS Pharmacy.
B. The IDS Pharmacy representative will promptly report to the HRPP Director of any concerns regarding the potential misuse of an investigational drug, agent, or biologic.

Attachments:
FDA Contacts for Obtaining Emergency IND and IDE
<table>
<thead>
<tr>
<th>Product</th>
<th>Contact</th>
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<tbody>
<tr>
<td>Drug Products</td>
<td>Drug Information Branch (HFD-210) (301) 827-4573</td>
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<tr>
<td>Biological Blood Products</td>
<td>Office of Blood Research and Review (HFM-300) (301) 827-3518</td>
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<tr>
<td>Biological Vaccine Products</td>
<td>Office of Vaccines Research and Review (HFM-400) (301) 827-0648</td>
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<tr>
<td>Biological Therapeutic Products</td>
<td>Office of Therapeutics Research and Review (HFM-500) (301) 594-2860</td>
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<tr>
<td>Nights and Weekends</td>
<td>Division of Emergency and Epidemiological Operations (HFC-160) (301) 443-1240</td>
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<tr>
<td>Devices</td>
<td>Center for Devices and Radiological Health (301) 594-1190</td>
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