

APPENDIX B

REQUIREMENTS AND PROCEDURES FOR THE EMERGENCY USE OF AN UNAPPROVED INVESTIGATIONAL DRUG, BIOLOGIC, OR DEVICE

A. Requirements for Emergency Use

Each of the following conditions must exist to justify the emergency use of an unapproved investigational drug (including a biologic) or device:

- 1) the patient has a life-threatening condition that requires immediate treatment;
- 2) no generally acceptable alternative for treating the patient is available; and
- 3) because of the immediate need to use the drug or device, there is not sufficient time to obtain IRB (i.e., full board) approval.

B. Requirements for an Investigational New Drug Exemption (IND) or an Investigational Device Exemption (IDE)

1) Investigational drug or biologic.

The emergency use of an unapproved investigational drug or biologic requires an IND (investigational new drug) exemption. If the intended subject/emergency use does not meet the criteria or methods of a research protocol being conducted under a currently approved IND for the drug or biologic, the investigator must contact the FDA to obtain prospectively permission for the emergency use under this IND. If there is currently no IND in place for the unapproved drug or biologic, the investigator must contact the FDA to obtain prospectively an Emergency IND number (see FDA Contacts for Obtaining an Emergency IND below). Alternately the emergency use may be conducted under an existing Treatment IND or Parallel Track IND.

2) Investigational device.

The emergency use of an unapproved investigational device does not require an IDE for such use, provided that the physician subsequently provides written justification to the FDA that an emergency actually existed.

3) General requirements.

In requesting an emergency use of a drug or biologic under an existing IND or an Emergency IND number, or notifying the FDA of the emergency use of an investigational device, the FDA expects the physician to determine whether the criteria for emergency use have been met, to assess the potential for benefits from the emergency use of the drug or device, and to have substantial reason to believe that benefits will exist. The physician may not conclude that an “emergency” exists in advance of the time when the treatment may be needed based solely on the expectation that IND or IDE approval procedures require more time than available. Physicians should be aware that the FDA expects them to exercise reasonable foresight with

respect to potential emergencies and to make appropriate, advance arrangements under Treatment IND, Parallel Track IND, or IDE procedures to avoid creating a situation where such arrangements are impracticable.

C. Procedures for the Emergency Use of an Unapproved Investigational Drug or Biologic

- 1) Contact the manufacturer of the investigational drug or biologic to determine if the manufacturer has in place a Treatment IND or a Parallel Track IND) that will permit emergency treatment of the patient outside a controlled clinical trial.
 - a) If yes, request inclusion of the patient in the Treatment IND or Parallel Track IND, request a supply (or a replacement supply if currently available under a controlled clinical study) of the drug for the emergency use, and obtain the Treatment or Parallel Track IND number.
 - b) If no, inquire if the manufacturer will provide a supply (or replacement supply) of the drug subsequent to obtaining FDA approval of the emergency use (i.e., if there is currently an approved IND for the drug or biologic) or an Emergency IND number (i.e., if there is no approved IND for the drug or biologic). Note that the manufacturer will likely require the attending physician to contact the FDA to obtain emergency use of Emergency IND approval, with subsequent notification of the manufacturer. To facilitate this process, request that the manufacturer identify the specific FDA Division which is currently reviewing the drug or biologic.

To obtain an emergency use approval under an existing IND or to obtain an Emergency IND number:

Product	Office/Division to Contact
Drug products	Division of Drug Information (HFD-240) 301-796-3400
Biological blood products	Office of Blood Research and Review (HFM-300) 301-827-3518
Biological vaccine products	Office of Vaccines Research (HFM-400) 301-827-3070
On nights and weekends	Office of Crisis Management & Emergency Operations center (HFC-160) 301-443-1240

- 2) Notify (412) 383-1480 during normal working hours; off-hours, follow audix instructions) the chairperson or a vice chairperson of the IRB of the intended emergency use of the unapproved investigational drug or biologic. (This notification should occur prior to implementation of the emergency use). Provide the IND number under which this use is authorized (e.g., Treatment IND, Parallel Track IND, other currently approved IND, or Emergency IND).

- If the unapproved investigational drug or biologic emits ionizing radiation, the Radiation Safety Office (412-624-2728) must also be notified.
- 3) Obtain written informed consent (see sample Emergency Use Consent Form on the IRB website) from the patient or the patient's legally authorized representative.
- a. Even for an emergency use, there is a provision for waiver of informed consent if both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:
- the subject is confronted by a life-threatening situation necessitating use of the test article.
 - 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.
 - no alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.
- b. If, in the investigator's opinion, there is not sufficient time to obtain an independent physician's determination that the four criteria are met, the investigator should make the determination and subsequently obtain (i.e., within five working days) a review of his/her determination by a physician not participating in the investigation.
- 4) Post-implementation of the emergency use:
- a) Within 72 hours of initial notification of the IRB chairperson or a physician vice chairperson, submit two copies of the following to the IRB Office.
- A cover letter indicating that the submitted materials are in response to the emergency use of an unapproved investigational drug or biologic.
 - A completed IRB Cover Sheet specifying the name of the involved patient in the title of the protocol and the IND number under which the emergency use was authorized.
 - The completed Emergency Use Consent Form signed and dated by the patient or the patient's legally authorized representative or written documentation from both the investigator as well as a physician independent of the clinical investigator that a waiver of consent was necessary based on the four points noted above.
 - A brief protocol that a) specifies the name of the involved patient in the title; b) documents the conditions justifying emergency use of the unapproved investigational drug or biologic; and c) provides a rationale for the emergency use of unapproved investigational drug or biologic (i.e., an assessment of potential benefits and why it was felt that these benefits may be realized in this specific patient).

- b) Submit promptly and documents that may be required by the manufacturer or FDA as a result of emergency use.
- Submit a copy of all such documents to the IRB Office
- c) Submit promptly to the IRB, manufacturer, and/or FDA follow up reports with respect to the subsequent outcome of the emergency use, including the occurrence of adverse events.
- d) Evaluate the likelihood of a similar need for emergency use of the unapproved investigational drug or biologic, and if probable, immediately initiate efforts to obtain prospective FDA (if not already in existence) and IRB approval of a Treatment IND or Parallel Track IND (if applicable).
- Note that FDA regulations and University policy require that any subsequent emergency use of the investigational drug at the institution have prospective IRB (i.e., full board) review and approval.
- 4) Procedures for the Emergency Use of an Unapproved Investigational Device
- a. Contact the manufacturer of the investigational device to determine if it has in place an Investigational Device Exemption (IDE) that will permit emergency use of the device on a patient outside of a controlled clinical trial.
- a) If yes, request inclusion of the patient in this emergency use IDE, request immediate shipment of the device if not already available, and obtain the corresponding IDE number.
- b) If no, inquire if the manufacturer will ship the device for emergency use if not already available. If the device is available, inform the manufacture of the intended emergency use of the device outside of the approved clinical protocol. Note that the manufacturer should contact the FDA upon such notification, however the manufacturer may require the attending physician to initiate FDA contact (Center for Devices and Radiological Health, Program Operation Staff, (301) 594-1190).
- b. Notify (412) 383-1480 during normal working hours; off hours, follow audix instructions) the chairperson or a vice chairperson of the IRB of the intended emergency use of the unapproved investigational device. (This notification should occur prior to implementation of the emergency use). Provide the IDE number under which this use is authorized, if available from the manufacture.
- If the unapproved investigational device emits ionizing radiation, the Radiation Safety Office (412-624-2728) must also be notified.
- c. Obtain written informed consent (see example of Emergency Use Consent Form) from the patient or the patient's legally authorized representative.
- d. Post-implementation of the emergency use:
- a) Within 72 hours of initial notification of the IRB chairpersons, submit two copies of the following to the IRB Office.

- A cover letter indicating that the submitted materials are in response to the emergency use of an unapproved investigational device.
 - The completed Emergency Use Consent Form signed and dated by the patient or the patient's legally authorized representative.
 - A brief protocol that a) specifies the name of the involved patient in the title; b) documents the conditions justifying emergency use of the unapproved investigational device (see A above); and c) provides a rationale for the emergency use of unapproved investigational device (i.e., an assessment of potential benefits and why it was felt that these benefits may be realized in this specific patient).
- b) If the manufacturer does not currently have in place an emergency use IDE for the device, notify (within 1 working day) the FDA (if not previously done) of the emergency use of the unapproved device. Submit promptly any documents that may be required by the manufacturer and/or FDA as a result of such emergency use.
- Submit a copy of all such documents to the IRB Office.
- c) Submit promptly to the IRB, manufacturer, and/or FDA follow up reports with respect to the subsequent outcome of the emergency use, including the occurrence of adverse events.
- d) Evaluate the likelihood of a similar need for emergency use of the unapproved investigational device, and if probable, immediately initiate efforts to obtain prospective FDA (if not already in existence) and IRB approval of an emergency use IDE.
- Note that FDA regulations and University policy require that any subsequent emergency use of the investigational device at the institution have prospective IRB (i.e., full board) review and approval.

Guidelines: Emergency Use Consent Form

Department or School Letterhead)

CONSENT TO AN EMERGENCY EXPERIMENTAL TREATMENT

"TITLE: "Emergency Treatment of Jane Smith Using ----"

Specify title of study. The title of the informed consent document for emergency experimental treatment must include the name of the involved patient.

RESPONSIBLE PHYSICIAN: John Doe, M.D.
 Professor of Cardiology
 Department of Medicine
 University of Pittsburgh
 Room 4231, Scaife Hall
 Pittsburgh, PA 15213
 Telephone : 412-647-XXXX

DESCRIPTION

1) *Specifically address:*

- a) the patient's diagnosis requiring emergency treatment;
- b) the conditions justifying emergency use of the experimental drug or device; that is:
 - *the patient has a life-threatening condition that requires immediate treatment, and*
 - *no generally acceptable alternative for treating the patient is available.*
- c) identity of the experimental drug or device, and the fact that its use for this treatment is "experimental";
- d) a rationale for the emergency use of the experimental drug or device (i.e., why it is felt that the experimental drug or device may be of benefit in this specific patient);

2) *List, in sequence, each of the specific procedures that will be performed for the purpose of the emergency experimental treatment. Do not include procedures that are performed as part of the subject's routine medical care. Indicate, where applicable:*

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- a) *the volume (in teaspoonfuls/tablespoonfuls or ounces) of blood to be drawn;*
- b) *the dose, route, and dosage schedule of the experimental drug and of any other drugs that will be used in the emergency treatment;*
- c) *all procedures associated with the use of the experimental device, including the number and frequency of patient exposures to these procedures;*
- d) *the FDA approval status of any other drugs or devices that will be used in the treatment; and/or*
- e) *complete descriptions of diagnostic or treatment procedures and the number of times each will be performed.*

3) *Indicate the expected period of time that the subject will be involved in the experimental treatment.*

RISKS AND BENEFITS

- 1) *Address all reasonably foreseeable risks (e.g., physical, psychological, legal, or economic) and discomforts. List expected side effects/adverse reactions associated with the experimental drug/device and their expected frequency of occurrence. Include the statement, "In addition to the adverse events listed, there may be unforeseen reactions or even death associated with the treatment use of any experimental drug or procedure." Indicate any special precautions taken to avoid or minimize such risks.*
- 2) *Include radiation risk statements (see Appendix D, C.4.), if applicable (i.e., the research study involves exposure to ionizing radiation):*

ALTERNATIVE TREATMENT:

Specify that:

- 1) *no generally acceptable alternative for treating the patient is available; and*
- 2) *an alternative is no additional treatment.*

NEW INFORMATION:

Incorporate the following standard statement:

You, or your representative, will be promptly notified if any new information, either good or bad, about this emergency experimental treatment develops during its course and which may cause you to change your mind about continuing to participate.

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COSTS AND PAYMENTS

Address if the patient, or his/her third-party insurance provider, will be billed for any of the listed emergency experimental procedures (i.e., procedures not constituting routine medical care). If applicable, the patient should be informed that certain third-party insurance providers would not fund care that is delivered as part of experimental care and that, under such circumstances, the patient will be held directly accountable for the charges. The patient should be provided with an estimate of these charges.

COMPENSATION FOR INJURY

Incorporate the following standard statements:

If done at UPMC facility:

In the event that this experimental treatment should directly cause you injury (i.e., injury independent of your current life-threatening condition), the UPMC will provide you with the necessary care for this injury. UPMC reserves the right to bill your third-party insurance provider for the cost of such care, and you may be billed for any costs your insurance does not cover. UPMC will not provide you with any additional compensation as the result of such injury.

CONFIDENTIALITY:

Incorporate the following standard statements:

You understand that any information about you or your emergency experimental treatment will be handled in a confidential (private) manner consistent with other hospital medical records. However, in unusual circumstances, your records may be inspected by appropriate government agencies or be released in response to an order from a court of competent jurisdiction. Scientifically trained and properly authorized employees of the Food and Drug Administration may inspect your records as a result of the use of an experimental drug (or device) for your treatment.

RIGHT TO WITHDRAW:

1) Incorporate the following standard statements:

You understand that you do not have to take part in this emergency experimental treatment and, should you change your mind, you can withdraw from the treatment at any time. Your other care and benefits will be the same whether you participate in this treatment or not. You also understand that you may be

Initials _____

RESPONSIBLE PHYSICIAN'S CERTIFICATION

I declare that I have personally discussed the above information with the patient or the patient's representative and answered any questions he/she may have:

Physician's Signature

Date

*Note that only the physician responsible for the emergency experimental treatment is permitted to sign the Responsible Physician's Certification.