EMERGENCY USE OF DRUGS OR BIOLOGICS

Under usual circumstances, the use of an investigational drug, device or biologic requires prior approval of the IRB. Rarely there are emergency circumstances where it is in the best interests of a patient for an investigational drug, device or biologic to be used without IRB review and approval. Emergency use is defined as the use of an investigational drug or biological product with 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)]. The emergency use provision in the FDA regulations [21 CFR 56.104(c)] is an exemption from prior review and approval by the IRB. The exemption, which may not be used unless all of the conditions described in 21 CFR 56.102(d) exist, allows for one emergency use of a test article without prospective IRB review. FDA regulations require that any subsequent use of the investigational product at an institution have prospective IRB review and approval. FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

Investigators should do the following:

1. Determine if the proposed use meets the regulatory definition for emergency use of an investigational drug or biologic [21 CFR 56.102(d)]. Emergency uses must meet ALL of the following criteria:

    - The subject has a disease or condition which is life-threatening (e.g., the likelihood of death is high) or severely debilitating (e.g., may cause irreversible morbidity, such as blindness, loss of limb, loss of hearing, paralysis or stroke);
    - The subject's disease or condition requires intervention with the investigational drug or biologic before review at a convened meeting of the IRB is feasible; and
    - No standard acceptable treatment is available.

2. Contact manufacturer of drug/biologic to determine if it can be provided under an existing IND or, if not available through the manufacturer, contact the FDA for an Emergency IND.

Practical Tips: ·

- Useful websites:·
    - FDA Information Sheet with specific steps: http://www.fda.gov/cder/cancer/singleIND.htm
    - How to fill out the 1571 and 1572 http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm071098.htm
    - Contacts at the FDA http://www.fda.gov/AboutFDA/ContactFDA/default.htm
- Sometimes the manufacturer will not entertain your request until you have IRB acknowledgement, i.e. the Insight/eIRB Emergency Use form reviewed and acknowledged by an IRB chair.

- "Piggybacking" onto another investigator's or sponsor's existing IND application is usually easier, because they will often have a "package" of documents to send you. They must list you as a co-investigator (sub-investigator) on their IND.

3. Contact the Partners Human Research Office at **617-424-4100** to notify them of planned emergency use of a drug or biologic.

- If you have never used a drug in this fashion, you are strongly encouraged to speak personally with an IRB chairperson and research pharmacist in order to assist you with the process (see specific contacts below). You have important regulatory and reporting requirements with the FDA and IRB that must be followed.
- There must be a staff physician (i.e. not a fellow or resident) responsible for emergency uses; who oversees and is responsible for the emergency use and completes all reporting requirements.

4. Contact the **MGH Pharmacy (617-726-2515) or BWH Investigational Drug Service (617-732-6410**) as soon as possible to inform them of the planned use and shipment of drug.

- If you are expecting an emergency use **might** be necessary, please contact the research pharmacy and IRB staff **during regular business hours**, in order to get the regulatory process underway. It is difficult if not impossible to attend to certain matters, such as contact with the FDA or manufacturers at night and on weekends.
- At both institutions there are specific research pharmacists with expertise in emergency uses who can assist you (see contacts below), including weekend coverage.
- If a protocol from any institution or manufacturer is being followed, or other reference information regarding the drug or biologic is available, a copy must be sent to the IRB and the pharmacy. Any information regarding drug use, indication, administration, dispensing instructions (dose, route, frequency, etc), and preparation instructions must be sent to the pharmacy. The pharmacy needs to verify what is being prepared and the responsible physician should have something in writing to this effect. The pharmacist must be able to verify that the written order is correct and that no transcription errors occurred, (i.e. 1 mg vs. 1gm) before the drug can be released from pharmacy.

5. Obtain informed consent from subject or if incompetent to give informed consent, the subject's legally authorized representative (next-of-kin).

- If the holder of the IND (i.e., sponsor or other local or distant physician) has an existing patient consent form that is made available, that form may be used. The IRB would prefer to review these forms in advance of their use, if time permits, though this may not be possible in an emergency situation. Whenever possible, written consent should be sought.
- If there is no existing consent form available from a sponsor or other IND holder, a clinical consent form should be used. Physicians should discuss with patients, or legally authorized representatives, the investigational nature of the proposed emergency treatment, the risks and benefits, and document these discussions in the medical record, in clinical notes, and in a clinical consent form.
- **An exception to the requirement for informed consent may be made** 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 (or severely debilitating) situation necessitating the use of the investigational drug or biologic;
- 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.

If, in the investigator's opinion, immediate use of the investigational drug or biological product, or unapproved medical device 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 above apply, the investigator should make the determination and, within 5 working days after the use of the investigational drug or biological product, or unapproved medical device, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

6. Investigational drugs should be delivered to the Research Pharmacies at the respective hospitals, with the responsible receiving physician's name and contact information clearly noted on the mailing label. Alert the pharmacy about the expected arrival of the drug.

7. The investigator must notify the Partners Human Research Committee (PHRC) within **5 working days** after the use of the investigational drug or biological product, or unapproved medical device. Submit completed Insight/eIRB Emergency Use Form within **5 working days** after the use of the investigational drug or biologic. The Emergency Use Form must be signed by the staff physician who requested to use the drug or biologic.

Practical Tip: Attach a brief letter with a clinical synopsis of the patient if the information does not fit into the form.

CONTACTS FOR EMERGENCY USES OF INVESTIGATIONAL DRUGS:

MGH IRB Chair

Elizabeth Hohmann MD
Office 617-724-7532
Lab 617-724-8625; 6-0886
Office 617-726-3812
Pager PHS 28390

If not available, see contacts at IRB website for other IRB chairs

MGH Research Pharmacists

Contact pharmacist covering your service; they can put you in touch with covering research pharmacist.

Shipping Address:

John Vetrano R Ph
Research Pharmacy
Massachusetts General Hospital
55 Fruit St
Boston, MA 02114
Ph 617-726-2515
Fax 617-724-5013

BWH IRB Chairs

Elizabeth Hohmann MD
Office 617-724-7532
Lab 617-724-8625; 6-0886
Office 617-726-3812
Pager PHS 28390

Julian Seifter MD
Office 617-732-7482
Pager PHS 11686

If not available, see contacts at IRB website for other chairs.

BWH Research Pharmacists

Investigational Drug Service Pharmacy
617-732-6410 (7am-8pm weekdays and 7am-5pm weekends)
IDS pharmacist on-call pager: 33672 (24 hours, 7 days)

Jon Silverman R Ph
Pager: 33784
Office: 617-732-6410

John Fanikos R.Ph.
Office: 617-732-7165
Cell: 617-605-3237
Pager: 11024
Main Pharmacy: 617-732-7153 (24 hours, 7 days)

Shipping Address:
IDS Pharmacy
Tower L2
75 Francis Street
Boston, MA 02115

Spaulding IRB Chair

Leslie Morse, DO
Office: 617-573-2200
Pager: 61153

Spaulding Research Pharmacist

Stephen Kolaczkowski
Office: 617-573-2287

Spaulding Pharmacy Director

Samir Kobeissi
Office: 617-573-2285
Pager: 61158 (24-hours, 7 days)