GUIDANCE: Emergency Use, Single Patient/Compassionate Use, Expanded Access for Drugs/Devices

Section I: Emergency Use Requests

Please review HRP-322 Worksheet Emergency Use to determine if the request meets this criteria.

Emergency use is defined as the use of an investigational drug, biological product or device 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.

A. For Use of a Drug:

1. If this is for an emergency use of a drug, FDA approval is required.
2. If emergency use of a drug, the study team must request and receive an emergency IND from the FDA, discuss the case with the ISMMS Investigational Drug Services (IDS) and the physician must notify the ISMMS IRB within five (5) working days after the use of the test article [21 CFR 50.23(c)] via a Reportable New Information (RNI) submission in RUTH with “eIND” in the title. The following documentation must be submitted in the RNI:
    a. Acknowledgement letter from the FDA
    b. Authorization for use from the sponsor in the form of an email message or letter.
    c. Consent template (template available in RUTH- HRP-506 Template Consent Document - Emergency or Compassionate Use)
    d. CV of the treating physician
    e. Investigator brochure/package insert of the investigational drug
    f. Supplemental materials including treatment plan and clinical history of the patient.
3. All applicable reporting obligations to the FDA must be shared with the PPHS via an RNI submission in RUTH (i.e. follow-up reports and annual reports)

B. For Use of a Device:

1. If this is for an emergency use of a device, FDA approval is not required.

2. The FDA expects the physician to make the determination that the patient's circumstances meet the criteria, to assess the potential for benefit from the use of the unapproved device, and to have substantial reason to believe that benefits will exist. In the event that a device is used in circumstances meeting the criteria listed above, the physician should follow as many patient protection procedures as possible. Such patient protection procedures include obtaining:
    a. Informed consent from the patient or a legal representative (template available in RUTH- HRP-506 Template Consent Document - Emergency or Compassionate Use)
    b. Clearance from the Institution as specified by their policies: contact Michael McCrary (Senior Vice President of Mount Sinai Health System, Administration.
    c. An independent assessment from an uninvolved physician
    d. Authorization from the device manufacturer via an email message or letter
    e. Concurrence from the Institutional Review Board (IRB) chairperson (this is done via a RUTH RNI submission)
3. If the situation meets the criteria for emergency use of a device, the treating team is instructed to submit an RNI to request IRB Chair concurrence. In an emergency use scenario of a device, IRB approval is not necessary but IRB Chair concurrence must be sought. The RNI submission in RUTH must include “eIDE” in the title, patient protection procedures noted above, a device brochure and CV of the treating physician. A letter will be issued once the IRB Chair provides concurrence.
4. All applicable reporting obligations to the FDA must also be shared with the PPHS via an RNI submission (i.e. follow-up reports and annual reports)

Section II: Non-Emergency Individual Patient Requests (also known as: Compassionate Use or Single Patient INDs)

A. For Use of a Drug:

These require an IND from the FDA. Typically these are cases where there isn’t a clinical trial that the person can enroll in and so the FDA must issue an IND in order for the drug to be shipped and for the physician to administer the drug.

The review time for an expanded access IND application intended for clinical treatment in non-emergency setting is 30 days following FDA’s receipt of the application. IRB concurrence or approval will not be granted until appropriate notification has been received from FDA.

A physician using Form FDA 3926 may choose to request alternative IRB review procedures (option 10b), which includes authorization to obtain concurrence by an IRB chairperson, or by a designated IRB member before the treatment use begins, in lieu of obtaining IRB review and approval at a convened IRB meeting at which a majority of the members are present. If "alternative review procedures" is not selected on Form FDA3926, a complete IRB application in RUTH is required.

If FDA approval is granted and IRB concurrence (option 10b) is selected on Form FDA 3926, a RNI may be submitted to request IRB chair concurrence.

In the RNI submission, the following must be provided and the RNI title must indicate "single patient compassionate use":

1. Form FDA3926 with alternative review procedures selected and submitted supplemental materials including treatment plan and clinical history
2. Acknowledgement from the FDA
3. Authorization from the sponsor in the form of email or letter.
4. Consent template (template available in RUTH- HRP-506 Template Consent Document - Emergency or Compassionate Use)
5. CV of the treating physician
6. Investigator brochure/package insert of the drug

Once IRB chair concurrence is granted, a letter (PDF) will be issued to the RNI submitter.

Please note IRB chair concurrence for drugs is valid for one (1) year. If the study team wishes to continue investigational treatment for this single individual for more than one year, IRB chair concurrence for continuing treatment must be sought. Please reach out to Jake Sutera (jake.sutera@mssm.edu) within four (4) weeks of your approval period to request continuing study treatment.

All applicable reporting obligations to the FDA must also be shared with the PPHS via a RNI submission (i.e. follow-up reports and annual reports)

B. For Use of a Device:

FDA device regulations are different than drug regulations. **FDA doesn't issue single patient IDEs.** It grants approval of a compassionate use request although there is still official documentation from the FDA. **FDA only issues IDEs for clinical trials, not for the use of an unapproved device for treatment purposes.**

This means that while a physician can create a protocol for a serial single patient IND situation, the same cannot be done for devices. Each request must be reviewed individually. FDA strongly *discourages* multiple compassionate use requests for the same device and *encourages* physicians to submit an application for an IDE and open a clinical trial instead - this does not mean that FDA will not grant a second compassionate use if requested.

FDA approval is required before using the investigational device on a subject.

The IDE sponsor (who may be the device manufacturer or a physician who has submitted the IDE to conduct the clinical study for the device) may submit to the FDA an IDE supplement requesting approval for a compassionate use under section §812.35(a) to treat the patient. The IDE supplement to the FDA should include:

1. A description of the patient's condition and the circumstances necessitating treatment;
2. A discussion of why alternative therapies are unsatisfactory and why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition;
3. An identification of any deviations in the approved clinical protocol that may be needed to treat the patient;
4. The patient protection measures that will be followed:
    a) A draft of the informed consent document that will be used (template available in RUTH- HRP-506 Template Consent Document - Emergency or Compassionate Use)
    b) Clearance from the institution as specified by their policies: contact Michael McCrary (Senior Vice President of Mount Sinai Health System, Administration.
    c) Concurrence of the IRB chairperson (this is done via the RUTH RNI submission)
    d) An independent assessment from an uninvolved physician; and
    e) Authorization from the device manufacturer on the use of the device.

A RNI must be submitted in RUTH (listing “compassionate use/single patient treatment” in the title) requesting IRB chair concurrence for this compassionate use that includes:

1. The FDA acknowledgement letter,
2. Patient protection procedures noted above,
3. A device brochure
4. CV of the treating physician.

Once concurrence is granted a letter (PDF) will be issued to the RNI submitter.

All applicable reporting obligations to the FDA must also be shared with the PPHS via a RNI submission (i.e. follow-up reports and annual reports)

Section III: Treatment Protocol for Large Groups

A. For Use of a Device:

Access to an investigational drug (including a biologic) for treatment use by a large (widespread) population, should be submitted as a protocol under a new IND. The investigational product must be under active development for marketing. Unless FDA notifies the sponsor that treatment may begin earlier, there is a 30-day waiting period before treatment may begin.

These protocols are submitted in RUTH as standard IRB submissions and are reviewed by either a convened IRB committee or sent to an external IRB.

B. For Use of a Device:

An approved IDE specifies the maximum number of clinical sites and the maximum number of human subjects that may be enrolled in the study. During the course of the clinical trial, if the data suggest that the device is effective, then the trial may be expanded under a new IDE to include additional patients with life-threatening or serious diseases. This is called a treatment IDE. Treatment use under a treatment IDE may begin 30 days after the FDA receives the treatment IDE submission. The FDA may notify the sponsor in writing earlier than the 30 days that the treatment use may or may not begin. The FDA may approve the treatment use as proposed or approve it with modifications.

These protocols are submitted in RUTH as standard IRB submissions and are reviewed by either a convened IRB committee or sent to an external IRB.