1 PURPOSE

1.1 This guidance establishes the process for treating physicians' requests for and the Sharp HealthCare (SHC) Institutional Review Board's (IRB) review of use of an investigational medical product (drug, biologic, or device) via one of the U.S. Food and Drug Administration's (FDA) Expanded Access pathways, including:

1.1.1 Proposed non-emergency, expanded access use of an investigational drug or investigational biologic

1.1.2 Proposed compassionate use of an investigational device with or without an Investigational Device Exemption (IDE)

1.1.3 Emergency use of an investigational drug, investigational biologic, or investigational device

1.2 The guidance begins when the SHC IRB receives a notification of a proposed or actual use of an investigational product via one of the expanded access pathways.

1.3 The guidance ends when a designated reviewer has acknowledged the closure of the expanded access activity after receipt of a status update with supporting documentation from the treating physician, indicating that expanded access use has ended.

2 REVISIONS FROM PREVIOUS VERSION

2.1 If applicable, previous versions are available in the Human Research Protection Program Change Log.

3 POLICY STATEMENT

3.1 Expanded Access Categories for use of an **investigational drug or investigational biologic** (i.e., not approved or cleared by the FDA for treatment outside of clinical trials; see https://www.fda.gov/news-events/expanded-access/expanded-access-categories-drugs-including-biologics) when the patient has a serious or life-threatening disease or condition, and no comparable or satisfactory alternative therapy options are available:

3.1.1 Individual Patient Access

3.1.1.1 Individual Patient Expanded Access Investigational New Drug (IND; also referred to as a Single Patient IND)

3.1.1.2 Individual Patient Expanded Access Protocol (also referred to as a Single Patient Protocol)

3.1.1.3 Individual Patient Access in an Emergency

- Emergency IND (also referred to as Individual Patient Access IND for Emergency use)
- Emergency Protocol (also referred to as Individual Patient Expanded Access Protocol for Emergency Use)

3.1.2 Intermediate-Size Patient Population Access

3.1.2.1 Intermediate-size Patient Population Expanded Access IND

3.1.2.2 Intermediate-size Patient Population Expanded Access Protocol

3.1.3 Expanded Access for Widespread Use

3.1.3.1 Treatment IND

3.1.3.2 Treatment Protocol

3.2 Expanded Access Categories for use of an **investigational medical device** (i.e., not approved or cleared by the FDA for treatment outside of clinical trials; see https://www.fda.gov/medical-devices/investigational-device-exemption-ide/expanded-access-medical-devices) when the patient has a serious or life-threatening disease or condition, and no comparable or satisfactory alternative therapy options are available:

3.2.1 Emergency Use

3.2.2 Compassionate Use (or Individual Patient/Small Group Access)

3.2.3 Treatment Investigational Device Exemption (IDE)

3.3 Emergency Use of an Investigational Product – In most cases, use of an investigational product via an expanded access pathway requires prospective review and clearance / approval from

the SHC IRB, prior to use. However, the FDA permits emergency use of investigational products as follows:

3.3.1 The one-time emergency use of an investigational product is permitted provided a patient is in a life-threatening situation in which no standard acceptable treatment is available, and when there is not sufficient time to obtain SHC IRB review and approval. Any subsequent use of the investigational product at the institution shall have prospective SHC IRB review and approval.

3.3.1.1 Whenever possible, the treating physician will notify the SHC IRB in advance of the proposed emergency use of an investigational product for a patient in a life-threatening situation.

3.3.2 The treating physician will consult with an independent physician (not involved in the patient's care) for the emergency use of a device.

3.3.3 Per *POLICY: Investigational Drugs and Biologics (43019.01),* in certain emergency situations where IND submission and/or SHC IRB approval is not possible, the FDA may authorize shipment of an investigational drug or investigational biologic product for a specified use in advance of the submission of an IND. For further details, refer to 21 CFR 56.104(c).

3.3.4 Per *POLICY: Investigational Devices (16509),* in emergency circumstances, approval for the emergency use of an investigational device shall be obtained from the IRB chair or designee.

3.3.5 Informed consent will be obtained from the patient or their legally authorized representative in advance of the investigational product, using an SHC IRB cleared/approved informed consent document (i.e., the investigational product manufacturer's informed consent template or *TEMPLATE: Consent - Emergency Use (HRP-506)),* unless the FDA's requirements for a waiver or exception from the informed consent requirement are satisfied and documented via *FORM: Exception from Informed Consent for Emergency Use (HRP-228)*.

3.3.6 The emergency use will be reported to the SHC IRB, using the *FORM: Emergency Use Notification (HRP-227)* with required supporting documentation, within five (5) working days.

3.3.7 The emergency use will be reported to the holder of the IND or IDE. If there is no IND or IDE, the emergency use will be reported to the FDA.

3.3.8 The SHC IRB and FDA acknowledge that it is inappropriate to deny emergency treatment to a second qualified individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue. Any emergency treatment to a second qualified individual must follow the same process as a first-time emergency use.

4 RESPONSIBILITIES

4.1 The Treating Physician, IRB Chair or designee, and IRB Specialist carry out these procedures.

5 PROCEDURE

5.1 Prior to contacting the SHC IRB, the treating physician:

5.1.1 Determines there are no available clinical trials for the patient – Wherever possible, an investigational product should be used as part of a clinical trial. Information on clinical trials can be found using FDA's clinical trials search tool or visiting www.ClinicalTrials.gov. When enrollment is not possible (e.g., patient ineligibility, lack of ongoing clinical trials) or enrollment in a clinical trial is not feasible (e.g., distance to a trial precludes access), expanded access may be an option for gaining access to an investigational medical product.

5.1.2 Confirms patient's current disease or condition qualifies for expanded access – The patient has either a serious or immediately life-threatening disease or condition and there is no available comparable or satisfactory alternative available for the patient (21 CFR 312.305(a) or 21 CFR 812.36(b)).

5.1.3 Identifies the appropriate expanded access pathway – For questions, contact the manufacturer (sponsor) of the investigational product and/or the appropriate FDA organization.

5.1.4 Confirms the manufacturer will provide investigational product – If the patient meets the criteria for expanded access, the treating physician will contact the manufacturer to see if they will provide the investigational product for expanded access use. Some resources for discovering availability of expanded access to investigational medical products may include:

5.1.4.1 Manufacturer Policy – Contact the manufacturer and find out if they are willing to provide the specific investigational product being sought for treatment purposes under expanded access.

5.1.4.2 Available Programs – Search for specific expanded access programs through an online search engine or the Reagan-Udall Foundation's Expanded Access Navigator.

5.1.4.3 Patient Advocacy Organizations – Contact patient advocacy organizations to see if they have information on expanded access programs for the patient's disease or condition.

5.2 After the treating physician gets the manufacturer's agreement to provide the investigational product for use outside of a clinical trial:

5.2.1 The treating physician:

5.2.1.1 Works with the manufacturer to initiate the appropriate application to the FDA for the expanded access use (see Expanded Access Categories for Drugs (Including Biologics), Emergency Use of an Investigational Drug or Biologic, or Expanded Access for Medical Devices)

- If the treating physician will be the sponsor, they submit an expanded access request to the FDA

5.2.1.2 Notifies the SHC IRB Office of their plan to use an investigational product via an expanded access pathway – Via research@sharp.com or via phone, the treating physician provides the following information to the SHC IRB:

- Expanded access type (see sections 3.1 through 3.3)
- IND number (drug, biologic) or IDE number (device), if available
- Name of the investigational product
- Name of the manufacturer
- Condition or disease the investigational product is intended to treat
- Patient's initials
- Date(s) of the proposed use or, in the case of an Emergency Use that has already occurred, the date(s) the investigational product was used

5.2.2 An IRB Specialist provides to the treating physician the forms and templates applicable to the expanded access pathway that was or will be followed

5.2.3 The treating physician submits to the SHC IRB Office the completed IRB forms, customized templates (i.e., informed consent), and required supporting documentation

5.2.4 Upon confirmation that the expanded access submission is complete and accurate, an IRB Specialist provides the documents to the IRB Chair or adds the submission to the next IRB meeting agenda

5.3 **Non-emergency use of an investigational drug, biological product, or device for a single patient**:

5.3.1 Applicable documents:

5.3.1.1 FORM: Single Patient Expanded Access to an Investigational Drug or Biologic (HRP-206) or *FORM: Compassionate Use of Device (HRP-205)*

5.3.1.2 FORM: Independent Physician Assessment (HRP-246)

5.3.1.3 WORKSHEET: IRB Chair Concurrence (HRP-335)

5.3.1.4 TEMPLATE LETTER: Expanded Access / Compassionate Use Clearance (HRP-522)

5.3.1.5 TEMPLATE: Consent – Expanded Access (HRP-506)

5.3.2 The treating physician will:

5.3.2.1 Facilitate the process - they will be responsible for managing the use of the investigational product and the patient's medical care. This includes:

- Reviewing the requirements for expanded access.
- Evaluating potential risks and potential benefits with the patient.
- Obtaining informed consent, consistent with Federal requirements under 21 CFR 50.
- If the treating physician will be the sponsor:
  - Submitting follow-up reports to FDA.
  - Submitting the expanded access protocol to SHC IRB that complies with the Federal IRB requirements under 21 CFR 56. The SHC IRB will be responsible for initial and continuing review and approval of the protocol.

5.3.3 Prior to use, the treating physician:

5.3.3.1 Contacts the manufacturer or sponsor to determine if the investigational product can be made available for the expanded access use under the company's IND (drug, biologic product) or IDE (device).

5.3.3.2 If the manufacturer does not permit use of the investigational product under their IND/IDE, the treating physician may request a single patient IND/IDE from the FDA by telephone, facsimile, or other means of electronic communication.

5.3.3.3 If the investigational product is a device, consults with an independent physician not involved in the patient's care and obtains a written assessment via *FORM: Independent Physician Assessment (HRP-246)* from them, confirming that the compassionate use criteria have been met.

5.3.3.4 Obtains IRB review and approval for the expanded access use, or requests authorization from the FDA under 21 CFR 56.105 using form FDA 3926 to obtain concurrence with the expanded access request from the IRB in lieu of complying with the requirements in 21 CFR 56.108(c), which relate to full IRB review. Concurrence can be requested by submitting for review: *FORM: Single Patient Expanded Access to an Investigational Drug or Biologic (HRP-206*) or *FORM: Compassionate Use of Device (HRP-205)* with the required supporting documents. An IRB Chairperson's concurrence with the proposed use is documented via *WORKSHEET: IRB Chair Concurrence (HRP-335)*.

- Note: Concurrence cannot be requested in place of full IRB review for Individual Patient Expanded Access Protocol (also referred to as a Single Patient Protocol) (see section 5.5).

5.3.3.5 Prior to treatment, the treating physician uses *TEMPLATE: Consent – Expanded Access (HRP-506)* to document authorization from the patient or their legally authorized representative. The treating physician provides a copy to the patient or their legally authorized representative.

5.3.3.6 Patients receiving an investigational product in an expanded access use as defined by FDA regulations may not be a research participant.

5.3.3.7 Data obtained from uses covered by this procedure cannot be used in a non-exempt systematic investigation designed to develop or contribute to generalizable knowledge. Such data cannot be classified as human subjects' research and the outcome of such care may not be permitted to be included in any report of a research activity subject to DHHS regulations.

5.4 **One-time emergency use of an investigational drug, biological product, or device**:

5.4.1 Applicable documents:

5.4.1.1 WORKSHEET: Emergency Use (HRP-322)

5.4.1.2 FORM: Emergency Use Notification (HRP-227)

5.4.1.3 FORM: Exception from Informed Consent for Emergency Use (HRP-228)

5.4.1.4 FORM: Independent Physician Assessment (HRP-246)

5.4.1.5 TEMPLATE LETTER: Emergency Use Acknowledgement Letter to Manufacturer (HRP-559)

5.4.1.6 TEMPLATE: Consent – Expanded Access (HRP-506)

5.4.2 The treating physician will assess the patient to determine the following criteria are met:

5.4.2.1 The patient to be treated has a serious or immediately life-threatening disease or condition.

5.4.2.2 There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition.

5.4.2.3 There is not sufficient time to obtain prior IRB review and approval.

5.4.2.4 The potential patient benefit justifies the potential risks of the treatment use, and those potential risks are not unreasonable in the context of the disease or condition to be treated;

5.4.2.5 The probable risk to the person from the investigational product is not greater than the probable risk from the disease or condition; and

5.4.2.6 The provision of the investigational product for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use.

5.4.3 Prior to emergency use, the treating physician:

5.4.3.1 Contacts the manufacturer or sponsor to determine if the investigational product can be made available for the emergency use under the company's IND (drug, biologic product) or IDE (device).

5.4.3.2 If the manufacturer does not permit use of the investigational product under their IND/IDE, the treating physician may request emergency use from the FDA by telephone, facsimile, or other means of electronic communication.[1]

5.4.3.3 Notifies an IRB on-call Chairperson to inform them of the intended emergency use and, if required by the manufacturer, request a *TEMPLATE LETTER: Emergency Use Acknowledgement Letter to Manufacturer (HRP-559)* from the IRB.

5.4.3.4 If the investigational product is a device, consults with an independent physician not involved in the patient's care and obtains a written assessment via *FORM: Independent Physician Assessment (HRP-246)* from them, confirming that the emergency use criteria have been met.

- If the treating physician determines that it is necessary to immediately treat the patient with the investigational product and there is not sufficient time to obtain the independent physician's determination, the treating physician should make the determination and, within five (5) working days after the use of the device, have the determination reviewed and evaluated in writing by an independent physician via *FORM: Independent Physician Assessment (HRP-246).*

[1] For emergency use of an investigational device when an individual patient is in a life-threatening situation and needs immediate treatment (there are no alternative options and no time to use existing procedures to get FDA approval for the use) FDA approval prior to use is not required; however, follow-up reports to the FDA are required.

5.4.3.5 When informed consent can be obtained, the treating physician uses *TEMPLATE: Consent – Expanded Access (HRP-506)* to document authorization from the patient or their legally authorized representative. The treating physician provides a copy to the patient or their legally authorized representative.

5.4.3.6 When informed consent cannot be obtained, FORM: Exception from Informed Consent for Emergency Use (HRP-228) is completed.

- FDA regulations permit emergency use of an investigational product without informed consent where the treating physician and an independent physician certify in writing:
  - The patient is confronted by a life-threatening or severely debilitating situation, necessitating the use of the investigational product.
  - Informed consent cannot be obtained from the patient because of an inability to communicate with, or obtain legally effective consent from, the patient.
  - Time is not sufficient to obtain consent from the patient's legally authorized representative.
  - No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the patient's life.

5.4.4 Patients receiving an investigational product in an emergency use as defined by FDA regulations may not be a research participant.

5.4.5 Data obtained from uses covered by this procedure cannot be used in a non-exempt systematic investigation designed to develop or contribute to generalizable knowledge. Such data cannot be classified as human subjects' research and the outcome of such care may not be permitted to be included in any report of a research activity subject to DHHS regulations.

5.4.6 For IRB notifications of the emergency use of an investigational product in a life-threatening situation, the designated reviewer uses the *WORKSHEET: Emergency Use (HRP-322)* to determine whether the circumstances will meet the regulatory and guidance criteria.

5.4.7 After emergency use, the treating physician:

5.4.7.1 Completes the *FORM: Emergency Use Notification (HRP-227)*, *FORM: Exception from Informed Consent for Emergency Use (HRP-228) (*if applicable) and submits to the IRB with a copy of signed informed consent (if applicable) with the patient's name obscured and replaced with their initials. Submit all required documents to the IRB within five (5) working days of the actual use of the investigational product.

5.4.8 For prospective IRB notifications of the emergency use of an investigational product in a life-threatening situation, the designated reviewer uses the *WORKSHEET: Emergency Use (HRP-322)* to determine whether the circumstances will meet the regulatory and guidance criteria and indicates the results of this determination to the treating physician using *TEMPLATE: EMAIL: Pre-Review of Emergency Use (HRP-570)*.

5.4.8.1 If met, inform the treating physician that the request has met regulatory criteria for emergency use and can proceed with the use.

- Use *TEMPLATE: Consent – Expanded Access (HRP-506)* for guidance on developing the informed consent.
- Use *FORM: Exception from Informed Consent for Emergency Use (HRP-228)* to determine if criteria for waiving consent is met.

5.4.8.2 If not met, inform the treating physician that if they proceed with the use, the IRB will consider that action to be Non-Compliance.

5.5 **Expanded access requests categorized as Individual Patient Expanded Access Protocol (also referred to as a Single Patient Protocol), Intermediate-Size Patient Population Access, Expanded Access for Widespread Use, and Treatment Investigational Device Exemption (IDE) the treating physician**:

5.5.1 Contacts the manufacturer or sponsor to determine if the investigational product can be made available for the expanded access use under the company's expanded access IND (drug, biologic product) or IDE (device).

5.5.2 Submits *FORM: Initial IRB Review Application (HRP-211)* with supporting documents for prospective IRB review following the process used for clinical trials.

6 MATERIALS

6.1 POLICY: Investigational Drugs and Biologics (43019.01)
6.2 POLICY: Investigational Devices (16509)
6.3 FORM: Compassionate Use of Device (HRP-205)
6.4 FORM: Single Patient Expanded Access to and Investigational Drug or Biologic (HRP-206)
6.5 FORM: Initial IRB Review Application (HRP-211)
6.6 FORM: Emergency Use Notification (HRP-227)
6.7 FORM: Exception from Informed Consent for Emergency Use (HRP-228)
6.8 FORM: Independent Physician Assessment (HRP-246)
6.9 WORKSHEET: Emergency Use (HRP-322)
6.10 WORKSHEET: IRB Chair Concurrence (HRP-335)
6.11 TEMPLATE: Consent - Emergency Use (HRP-506)
6.12 TEMPLATE LETTER: Expanded Access / Compassionate Use Clearance (HRP-522)
6.13 TEMPLATE LETTER: Emergency Use Acknowledgement Letter to Manufacturer (HRP-559)
6.14 TEMPLATE EMAIL: Pre-Review of Emergency Use (HRP-570)

7 REFERENCES

7.1 21 CFR 50.23; 21 CFR 56.104(c); 21 CFR 56.105; 21 CFR 56.108(c)
7.2 21 CFR 50.23 – Exception from general requirements for informed consent
7.3 21 CFR 56.102(d) – Emergency Use definition
7.4 21 CFR 312 Subpart I – Expanded Access to Investigational Drugs for Treatment Use
7.5 21 CFR 812.35; 21 CFR 812.36 – Treatment use of an investigational device
7.6 https://www.fda.gov/news-events/expanded-access/expanded-access-categories-drugs-including-biologics
7.7 https://www.fda.gov/medical-devices/investigational-device-exemption-ide/expanded-access-medical-devices

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