1. PURPOSE
   1. This procedure establishes the process to assist treating physicians with the FDA requirements for emergency use of a test article in a life-threatening situation.
2. POLICY
   1. **Emergency Use** means the use of a test article 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.
   2. Each of the following conditions must exist to justify emergency use of a drug or biologic:
      1. the patient is in a life-threatening or severely debilitating condition that needs immediate treatment;
      2. no generally acceptable alternative for treating the patient is available; and
      3. because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.
   3. **Life-threatening** means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted, as well as diseases or conditions with potentially fatal outcomes. The criteria for a life-threatening disease or condition does not require the condition to be immediately life threatening or to immediately result in death. Rather the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.
   4. **Severely Debilitating** means diseases or conditions that cause major irreversible morbidity including blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.
   5. **Test article** means any [investigational] drug, biological product, or medical device for human use.
   6. The FDA regulations [21 CFR 56.104(c)] allow for **one** emergency use of a test article without prior review and approval by the IRB. FDA regulations require that any subsequent use of the investigational product at the 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.
   7. Data obtained from uses covered by this procedure cannot be used for any research purposes.
3. RESPONSIBILITIES
   1. The treating physician/principal investigator is responsible to ensure these procedures are carried out.
4. PROCEDURE When Using an Investigational Drug or Biologic:
   1. Whenever possible, physicians are required to notify the IRB immediately if they are considering using an investigational article in an emergency use situation in order to:
      1. Confirm that the disease or condition is either serious or immediately life threatening;
      2. Confirm that there is insufficient time for the IRB to review and approve the investigational use;
      3. Determine if an IND must be obtained from the FDA as required under 21 CFR 312.310;
         1. If the use of the unapproved test article does not meet the criteria of an existing study protocol or if an approved study protocol does not exist, the investigator/clinician must contact the manufacturer of the test article and determine if it can be made available for emergency use under the manufacturer’s IND.
         2. If the manufacturer is unwilling to sponsor the emergency use through its IND, and there is no time for the investigator to submit an IND, the investigator must obtain the FDA’s authorization and the manufacturer’s agreement to ship the unapproved test article.
   2. The proposed use or use of the test article must be reported to the IRB via the PRISM system (include ‘Emergency Use of Drug/Biologic in title of submission) as soon as possible, but no later than 5 days after the use of the test article. An email with Emergency Use of Drug/Biologic on the Subject Line must be sent to irb@carilionclinic.org to alert the IRB of this submission.
      1. Failure to do so may be considered Non-Compliance
   3. The IRB PRISM submission for Emergency Use must include:
      1. Emergency Use IND number or Authorization from the FDA to ship the investigational drug; and
      2. Approval from the Sponsor for use of the investigational product; and
      3. Justification as to the justification of the patient meeting the criteria in 2.2 above
      4. Documentation of the patient’s status after administration of the investigational product (if applicable); and
      5. The consent form that will be used or was used to consent the patient, or, if informed consent was unable to be obtained from the patient or his/her legally authorized representative, a letter from a physician not otherwise participating in the intervention certifying that:
         1. The patient was confronted by a life-threatening situation necessitating the use of the test article
         2. Informed consent could not be obtained because of an inability to communicate with or obtain legally effective consent from the patient
         3. Time was not sufficient to obtain consent from the patient’s legal representative
         4. No alternative method of approved or generally recognizable therapy was available that would provide an equal or greater likelihood of saving the patient’s life.
   4. Full Board approval is normally required for emergency use of a test article. If it is not feasible to convene a quorum before the treatment must be administered, then the emergency use may proceed without IRB approval only with advance notification to the IRB Office and review by the IRB Chair.
   5. IRB approval or concurrence for emergency use of a drug or biologic or a medical device will occur only if conditions in WORKSHEET: Emergency Use are met.
   6. If the IRB approves or the Chairperson concurs with the emergency use, then:
      1. The IRB Office/IRB Chair will notify the physician seeking emergency use approval or concurrence
      2. The IRB will use the date of concurrence to initiate tracking to ensure the investigator provides a report to the IRB within 5 working days as required by 21 CFR 56.104(c) and again at 30 days after use of the test article.
   7. For any emergency use, the investigator is required to obtain informed consent of the subject or the subject’s legally authorized representative. When legally effective consent cannot be obtained, the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following (21CFR50.23(a)):
      1. The subject is confronted by a life-threatening or severely debilitating situation necessitating the use of the test article;
      2. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from the subject;
      3. Time is not sufficient to obtain consent from the subject’s legally authorized representative; and
      4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject’s life or preventing a severely debilitating condition.
   8. If the investigator cannot obtain the independent assessment of a physician to certify the above, then within 5 days after the use of the test article, a physician who is not otherwise participating in the clinical investigation must certify with the investigator, in writing, that the above criteria were satisfied.
   9. For each subject unable to provide informed consent, the clinical investigator participating in emergency research must commit to attempting to seek written informed consent within the therapeutic window, if feasible, from the subject’s legally authorized representative. If no LAR is available, the clinical investigator must commit to attempting to contact a family member to provide an opportunity to object to the participation of an individual, before administering the test article without informed consent, if feasible.
   10. FDA and the IRB expect the physician to follow as many subject protection procedures as possible. These include:
       1. obtain IRB approval or the concurrence of the IRB Chair; and
       2. obtaining authorization from the IND/IDE holder, if applicable; and
       3. obtaining an independent assessment in writing, documented in the patient/subject’s medical record by an uninvolved physician; and
       4. obtaining informed consent from the patient or a legal representative; and
       5. notifying institutional officials as specified by institutional policies; and
       6. consider video monitoring or use a witness to the consent process.
   11. After emergency use, the investigator is required to:
       1. Monitor the patient to detect any possible problems arising from the use of the investigational article. This report will be reviewed by the Chair or Vice-Chair.
       2. Submit a 5 day follow-up report and 30 day follow-up report to the IRB, the Sponsor and/or the FDA in which summary information regarding the patient outcome is presented.
       3. Evaluate the likelihood of a similar need for the unapproved test article occurring again, and if future use is likely, immediately initiate efforts to obtain IRB approval of a study protocol to permit clinical use of the investigational drug.
       4. If an unanticipated problem involving risk to subjects or others (e.g., an SAE that was unexpected and related) occurred in connection with the emergency use, submit reports consistent with the reporting requirements of the IRB, the FDA, and the manufacturer of the test article.
       5. If the manufacturer agreed to sponsor the emergency use through its IND, provide the manufacturer with a written summary of the conditions constituting the emergency, subject protection measures, and the results of the emergency use.
       6. If the manufacturer did not agree to sponsor the emergency use through its IND, provide the FDA and the manufacturer with a written summary of the conditions constituting the emergency, subject protection measures, and the results of the emergency use within a formal IND application.
          1. Notes: (1) If the investigator submits a formal IND application, they must submit annual reports per FDA regulations. (2) If the investigator does not plan to write a formal protocol for use of the test article, they must submit a final report requesting withdrawal of the IND per FDA regulations
5. PROCEDURE for Emergency Use of an Unapproved Device
   1. Whenever possible, physicians are required to notify the IRB immediately if they are considering using an investigational article in an emergency use situation in order to:
      1. Confirm that the disease or condition is either serious or immediately life threatening;
      2. Confirm that there is insufficient time for the IRB to review and approve the investigational use;
      3. Determine if an IDE must be obtained from the FDA as required under 21 CFR 312.310;
         1. If the use of the unapproved test article does not meet the criteria of an existing study protocol or if an approved study protocol does not exist, the investigator/clinician must contact the manufacturer of the test article and determine if it can be made available for emergency use under the manufacturer’s IDE
         2. If the manufacturer is unwilling to sponsor the emergency use through its IDE, and there is no time for the investigator to submit an IDE, the investigator must obtain the FDA’s authorization and the manufacturer’s agreement to ship the unapproved test article.
   2. The proposed use or use of the device must be reported to the IRB via the PRISM system (include ‘Emergency Use of Device in title of submission) as soon as possible, but no later than 5 days after the use of the test article. An email with Emergency Use of Device on the Subject Line must be sent to irb@carilionclinic.org to alert the IRB of this submission.
      1. Failure to do so may be considered Non-Compliance
   3. The IRB PRISM submission for Emergency Use must include:
      1. Emergency Use IDE number or Authorization from the FDA to ship the investigational article; and
      2. Approval from the Sponsor for use of the investigational product; and
      3. Justification as to the justification of the patient meeting the criteria in 2.2 above
      4. Documentation of the patient’s status after administration of the investigational product (if applicable); and
      5. The consent form that will be used or was used to consent the patient, or, if informed consent was unable to be obtained from the patient or his/her legally authorized representative, a letter from a physician not otherwise participating in the intervention certifying that:
         1. The patient was confronted by a life-threatening situation necessitating the use of the test article
         2. Informed consent could not be obtained because of an inability to communicate with or obtain legally effective consent from the patient
         3. Time was not sufficient to obtain consent from the patient’s legal representative
         4. No alternative method of approved or generally recognizable therapy was available that would provide an equal or greater likelihood of saving the patient’s life.
   4. An investigator, who must be a licensed physician, may treat a patient with an unapproved medical device in an emergency situation if they conclude that:
      1. the patient has a life-threatening condition that needs immediate treatment (the criteria of “life-threatening condition”
      2. no generally acceptable alternative treatment for the condition exists; and because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.
   5. Prior to the emergency use, an investigator should meet as many of the following requirements as is practicable given the urgency of the clinical situation:
      1. Obtain IRB approval or the concurrence of the IRB Chair; and
      2. Obtain the assessment, in writing, of a physician who is not participating in the study or in the care of the patient that concurs with the planned usage; and
      3. Obtain the informed consent from the patient or their legal representative; and
      4. Authorization from the IDE sponsor, if an IDE exists for the device.
   6. If any of the requirements listed in 5.5 cannot be met due to the urgency of the clinical situation, the investigator must document in writing their reasons for proceeding.
   7. If the informed consent of the subject cannot be obtained prior to use of the device, the investigator must certify that all of the following have been documented in writing in the subject’s medical record:
      * 1. The subject is confronted by a life-threatening situation necessitating the use of the test article (device);
        2. Informed consent cannot be obtained because of an inability to communicate with or obtain legally effective consent from the subject;
        3. Time is not sufficient to obtain consent from the subject’s legally authorized representative;
        4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject’s life.
   8. After emergency use, the investigator is required to:
      1. Monitor the patient to detect any possible problems arising from the use of the investigational device. This report will be reviewed by the Chair or Vice-Chair.
      2. Submit a 5 day follow-up report and 30 day follow-up report to the IRB, the IDE Sponsor and/or the FDA. The report should contain a summary of the conditions constituting the emergency, patient outcome information, and the patient protection measures that were followed.
         1. If it was not possible to obtain informed consent prior to the emergency use, the report must include the determination to proceed as documented by a physician independent of the clinical investigation.
         2. The report of the independent physician’s findings must be submitted to the IRB along with the investigator’s report.
      3. Evaluate the likelihood of a similar need for the unapproved device occurring again, and if future use is likely, immediately initiate efforts to obtain IRB approval of a study protocol to permit clinical use of the investigational device. A second use of an unapproved device may not take place until approval of an IDE for the proposed use has been issued by the FDA.
      4. If an unanticipated problem involving risk to subjects or others (e.g., an SAE that was unexpected and related) occurred in connection with the emergency use, submit reports consistent with the reporting requirements of the IRB, the FDA, and the manufacturer of the test article.
6. MATERIALS
   1. [FDA Guidance on Treatment Use of Investigational Drugs](https://www.fda.gov/RegulatoryInformation/Guidances/ucm126495.htm) [FDA Guidance on IDE Policies and Procedures](https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080202.htm)
   2. [FDA Guidance on Emergency Use of an Investigational Drug or Biologic](https://www.fda.gov/RegulatoryInformation/Guidances/ucm126491.htm) - Information Sheet [Frequently Asked Questions about Medical Devices](https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM127067.pdf) – Information Sheet
   3. [Exception from Informed Consent Requirements for Emergency Research](http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM249673.pdf)
   4. [Guidance on IDE Policies and Procedures, Chapter III, Emergency Use of Unapproved Medical](https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080202.htm) [Devices](https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080202.htm)
7. REFERENCES
   1. 21 CFR §50.27
   2. 45 CFR §46.117
8. REVISIONS FROM PREVIOUS VERSION
   1. none