SPECIFIC INFORMATION

Regulations pertaining to emergency use of a test article (FDA-regulated investigational drug, biologic or device) are those of the US Food & Drug Administration (FDA), published as part of the Code of Federal Regulations (CFR) 21 CFR 50 and 21 CFR 56. Emergency use of a test article in a life-threatening condition is not considered research; nevertheless, it is under the purview of the IRB, because the use of an investigational test article not yet approved by the FDA is involved. The investigational drug or biologic must have received an IND (Investigational New Drug) approval, or the investigational device an IDE (Investigational Device Exemption) from the FDA for clinical testing, to be eligible for use in an emergency setting. Usually, IND or IDE acquisition is conducted by the manufacturer. If IND or IDE approval by the FDA is not available, the Investigator must contact the FDA on an emergency basis.

For emergency use of a test article, all of the following criteria must be met:

1. The subject is facing a life-threatening condition, for which there is no conventional treatment, or conventional treatments have failed.

2. The physician has access to a test article, and believes that there is a reasonable likelihood that the article will help save the subject’s life, and that there is no approved treatment that has equal or greater likelihood of helping the subject.

3. Comprehensive written informed consent is to be executed prior to initiation of the administration of the test article.

Certain emergency circumstances may not permit the execution of the standard informed consent process prior to administration of the test article. FDA regulations provide an exemption from the informed consent requirement, if the subject is unable to provide effective consent, and there is insufficient time in which to obtain consent from the subject’s legal representative. Under these circumstances, the opinion of another impartial physician is required on the expected benefit from the use test article; please refer to the “Definitions and interpretations of the Federal rules on Emergency Use of A Test article, prepared by the Office for Human Research Protections of the US Department of Health and Human Services”

The test article is expected to be administered to a single subject as a single course (may involve multiple dosing to achieve maximal efficacy). The subject to receive the test article should not be enrolled in a research study related to the test article. If subsequent use of the test article is contemplated in the same subject or in others, a new project application to the IRB is required in advance of that use.

The use of a test article in an investigation designed to be conducted under emergency conditions (e.g. emergency room research) usually does not qualify for the emergency use exemption.

Emergency use is defined as the use of a test article on 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 for the use. The Investigator is still required to obtain informed consent under these circumstances.
FDA exempts from IRB review the emergency use of a test article so long as the emergency use is reported to the IRB within five working days of its occurrence. Any subsequent use of the test article is subject to IRB review [21 CFR 50.23; 21 CFR 56.104(c)]. "Subsequent use" means any use of the test article that occurs after its initial emergency use. When an IRB receives a report by a clinical Investigator of an emergency use, the IRB must examine each case to assure itself and the institution that the emergency use was justified.

Although 21 CFR 56.104 is designed to permit only a single emergency use of a test article for the treatment of one patient by one physician within an institution, the regulation is not intended to limit the authority of a physician to provide emergency care in a life-threatening situation. Should a situation arise which would require the emergency use of the test article for a second patient, either by the same or a second physician, subsequent emergency use should not be withheld for the purpose of gaining IRB approval. If it appears probable that similar emergencies will require subsequent use of the test article at the institution, every effort should be made either to sign on to the Sponsor's protocol or to develop a protocol for future emergency use of the article at the institution. Either of these protocols would need to be prospectively reviewed and approved by the IRB for future use of the test article.

In emergency circumstances, it may not be feasible to obtain informed consent prior to using the test article. The regulations therefore provide an exemption from the informed consent requirement for such situations. Emergencies qualifying for this exemption are defined as:

1. life-threatening situations necessitating use of the test article;
2. where the subject is unable to provide effective consent;
3. there is insufficient time in which to obtain consent from the subject's legal representative; and
4. there is no available alternative method of approved or generally recognized therapy of equal or greater likelihood of saving the subject's life [21 CFR 50.23(a)(1)-(4)].

Special procedures for documenting the unfeasibility of obtaining consent apply as follows:

1. The Investigator and another physician, who is not participating in the clinical investigation, must certify in writing the existence of all four conditions listed above before use of the test article [21 CFR 50.23(a)].
2. If in the Investigator's opinion,
   a. immediate use of the test article is necessary to save the life of the subject; and
   b. there is insufficient time to obtain the independent determination required by 21 CFR 50.23(a) before using the test article;
   c. the Investigator is to make his or her own written determinations, then obtain the written review and independent evaluation of a physician who is not participating in the clinical investigation within five working days after the use of the test article [21 CFR 50.23(b)].

The documentation required by either 21 CFR 50.23(a) or 50.23(b) must be submitted to the IRB within five working days after the use of the test article [21 CFR 50.23(c)]
## REPORT OF EMERGENCY USE OF A TEST ARTICLE TO TREAT A LIFE-THREATENING CONDITION

**Investigator:**

**Study Title**

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1. **Physician**

   Title of research project:

   Emergency use of TEST ARTICLE in a single patient facing a life-threatening condition.

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2. **SPONSOR / FUNDING INFORMATION**

   Is this protocol supported by an external funding agency?  
   - [ ] No  
   - [x] Yes

   If yes, provide **Grant Review Form**

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3. **WHERE DID THE EMERGENCY USE TAKE PLACE?**

   - [ ] Hospital (Name)  
   - [ ] Private Practice (Name)  
   - [ ] Agency (Name)

   - [ ] Clinic (Name)  
   - [ ] Public area  
   - [ ] Other

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4. **PATIENT INFORMATION**

   - [ ] Male  
   - [ ] Female

   Name of Patient: __________________________

   Date of birth: __________________________

   Medical record number: __________________________

   Ethnicity/race: __________________________

   **Was the patient any of the following potentially vulnerable groups?**

   - [ ] Prisoners  
   - [ ] Mentally retarded /impaired  
   - [ ] Nursing home resident

   - [ ] Fetuses  
   - [ ] Economically disadvantaged  
   - [ ] Students

   - [ ] Pregnant women  
   - [ ] Investigator's staff member  
   - [ ] Homeless

   - [ ] Investigator's patient  
   - [ ] Other (describe)
5. DESCRIPTION OF LIFE THREATENING CONDITION

A Diagnosis

B Why was the condition considered life-threatening?
What were the symptoms and signs that made the physicians conclude that the patient was facing a life-threatening condition?

C What made the physicians conclude that there was no standard acceptable treatment available, so that an investigational treatment had to be offered?

D On what date did the administration or application of the test article to the patient begin, and when did it or will it end?

6. IS THE TEST ARTICLE REGULATED BY FDA?  0 No  0 Yes

If yes, complete this section

A 0 This study involves a drug or biologic: IND #, if applicable: ____________

This study is: Phase 1 0  Phase 2 0  Phase 3 0  Phase 4 0  Treatment 0

B 0 This study involves a device:

This device is 0 Investigational 0 Marketed

This is a 0 Significant Risk Device Study 0 Non-Significant Risk Device

C Who is the Sponsor of the IND/IDE?

D What was the generic name and/or code name of the test article?

E What was the source (supplier or manufacturer) of the test article?

F How did the physicians gain possession of the test article?

G What is the proposed mechanism of action of the test articles?

H If the test article is a drug, what is the drug trial phase status, as assigned by the FDA?

I If the test article is a device, what is the significant risk or nonsignificant risk device status, as assigned by the FDA?

J What was the dosage, route of administration or application, and frequency & total duration of use of the test article?
7. **COSTS**
   A **Study procedures and products**
   Will the patient or his/her health care provider be required to pay for any related procedures or products? If yes, explain:
   0 No 0 Yes

   B **Compensation for injury**
   Who is responsible for costs incurred due to adverse events?

8. **RISKS**
   A Identify the risks (current and potential).
   B Describe the expected frequency, degree of severity, and potential reversibility.
   C Describe possible late effects.
   D Risks from study article:
   E Risks from research procedures (i.e., washout risks, placebo assignment, etc.).
   F How will subjects be assessed for the occurrence of adverse events described above?
   H Describe your monitoring plan.
   I What information is available on the response of the patient’s life-threatening condition to the test article at the time of this report?

9. **FOLLOW-UP PROCEDURES**
   A What will be the duration of subjects’ active participation?
   B Will the patient be followed after their active participation ends? 0 No 0 Yes
   If yes, describe:

10. **INFORMED CONSENT**
    A What type of informed consent process was implemented prior to administration or application of the test article to the patient?
**REPORT OF EMERGENCY USE OF A TEST ARTICLE**

<table>
<thead>
<tr>
<th>B</th>
<th>Was the patient able to give informed consent?</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>If the mental acuity of the patient was in doubt, the person who gave the informed consent was:</td>
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<td></td>
<td>Legally appointed guardian</td>
<td>0</td>
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<td></td>
<td>Patient advocate named in a Durable Power of Attorney for Health Care</td>
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<td></td>
<td>Next-of-kin:</td>
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<td></td>
<td>Spouse</td>
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<td></td>
<td>Adult child</td>
<td>0</td>
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<td></td>
<td>Parent</td>
<td>0</td>
<td></td>
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<td></td>
<td>Adult brother/sister</td>
<td>0</td>
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<td>D</td>
<td>If the patient was age &lt;18 years, did he or she provide assent?</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>E</td>
<td>How will pertinent information be provided to the patients, if appropriate, at a later date? Describe or attach your debriefing plan.</td>
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<td>F</td>
<td>Who explained the study to the patient?</td>
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<tr>
<td>G</td>
<td>If circumstances prevented obtaining informed consent, explain why the patient was unable to provide effective consent; and why there was insufficient time in which to obtain consent from a legal representative of the patient.</td>
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<td>H</td>
<td>Please submit the informed consent document used or to be used. If already executed, please provide a copy of the document that bears signatures of the patient or his/her legal representative, the Investigator (or designee) providing information and others (as applicable) witnessing the consent.</td>
<td>See consent form template.</td>
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</tbody>
</table>

**11. CONFIDENTIALITY**

| A | Are the subject’s social security number, hospital record number, or any identifier (other than study number & initials) being sent off site? If yes, describe and explain reasons. | No | Yes |
| B | Will any external entity other than the investigative staff have access to or be provided with confidential medical or health related information about the subject. | No | Yes |

**12. EXPLANATION OF REPORTING DELAY**

If the interval between the date of initial administration of the test article and the date of submission of this application is more than five days, what was the reason for the delay in reporting?

<p>| Physician administering the test article | Date | Time |
| Concurring physician (if consent is not obtained) | Date | Time |</p>
<table>
<thead>
<tr>
<th>The protocol is under a separate investigational new drug application (IND) or investigational device exemption (IDE).</th>
<th>Yes</th>
<th>No</th>
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</thead>
<tbody>
<tr>
<td>The protocol clearly identifies that the research may include subjects who are unable to give informed consent.</td>
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<tr>
<td>The human subjects are in a life-threatening situation that requires intervention, and</td>
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<td>Available treatments are unproven or unsatisfactory, and</td>
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<tr>
<td>The collection of valid scientific evidence is necessary to determine the safety and effectiveness of particular interventions, and</td>
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<td>The clinical investigation could not practicably be carried out without the waiver of informed consent:</td>
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<tr>
<td>The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and</td>
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<tr>
<td>There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.</td>
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<tr>
<td>There is evidence that participation in the research holds out the prospect of direct benefit to the subjects:</td>
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<tr>
<td>Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and</td>
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<tr>
<td>Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.</td>
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<td>The protocol defines the length of the potential therapeutic window based on scientific evidence.</td>
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<tr>
<td>The IRB has reviewed and approved informed consent procedures and an informed consent document to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.</td>
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<tr>
<td>The protocol includes documentation that the Investigator will make every reasonable effort to obtain informed consent within the therapeutic window by:</td>
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<tr>
<td>Attempting to contact a legally authorized representative for each subject and obtain consent within the therapeutic window.</td>
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<tr>
<td>If a legally authorized representative is not reasonably available, attempting to contact, within the therapeutic window, the subject’s family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation.</td>
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</tbody>
</table>
Procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document.

That he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.

Procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with regulations are acceptable.

The Investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible.

Community disclosure and consultation will be carried out.

Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn will be carried out.

Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits.

Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results.

An independent data monitoring committee to exercise oversight of the clinical investigation will be established.