EMERGENCY USE OF A TEST ARTICLE

1.0 POLICY

1.1 Background

1.1.1 The University of Alabama recognizes that situations may arise in which investigators may deem it humane to depart from the rigor of an approved protocol to extend access to a medical treatment, drug, regimen, or device (collectively known as “test articles”) to those who might not otherwise qualify for participation in said protocol.

1.1.1.1 FDA regulations recognize emergency use of a test article in situations deemed life threatening (21 CFR 56.102 (d), Attachment 7-5-FDA Guidance on Research in Emergency Situations, http://www.nihtraining.com/ohsrsite/irb/Attachements/7_5_FDA_Emergency+Use.htm).

1.1.1.2 “Test Article” means any drug, biological product, or medical device for human use [21 CFR 56. 102(1)].

1.1.1.3 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.

1.1.1.4 Life-threatening means diseases where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes where the end point of clinical trial analysis is survival. It is not required 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.

1.1.1.5 Severely debilitating means diseases or conditions that cause major irreversible morbidity, such as blindness, loss of arm leg, hand or foot, loss of hearing, paralysis or stroke.

1.1.2 DHHS specifically recognizes that 45 CFR 46 will not override the authority of physicians to provide emergency medical care.

1.1.3 The emergency use of a test article, other than a medical device, is a clinical investigation, the patient is a participant, and the FDA may require data from an emergency use to be reported in a marketing application.
1.1.3.1 DHHS regulations do not permit data obtained from patients to be classified as human participants research, nor permit the outcome of such care to be included in any report of a research activity subject to DHHS regulations.

1.1.4. Consent will be obtained in accordance with FDA regulations, or the circumstances meet the exception to the requirement for consent in FDA regulations.

1.1.4.1 Informed consent is sought from each perspective participant or the participant’s legally authorized representative, in accordance with and to the extent required by 21 CFR 50 [The consent process needs to disclose all required and appropriate additional elements of consent disclosure.].

1.1.4 This policy does not apply to planned research in life-threatening emergencies covered by 21 CFR §50.24 in which the research plan is approved in advance by the FDA or DHHS and publicly disclosed to the community where the research will be conducted. The University of Alabama does not conduct planned emergency research or review requests for a waiver of the requirement for consent for planned emergency research.

1.1.5 When following Department of Defense regulations and requirements, an exception from consent in emergency medicine research is prohibited unless a waiver is obtained from the Secretary of Defense.

1.2 Policy Statement

It is the policy of the University of Alabama that study investigators may apply investigational drugs (if the research involves an investigational drug and the FDA has issued an IND), agents or biologics or medical devices in the treatment of persons who are in a life-threatening situation. All instances of emergency use must be accompanied by a written justification provided to the IRB by the Investigator within 5 working days of the instance of use.

1.2.1 The application of emergency use of a test article will be limited to those situations where at least one of the following characterizes the disease or condition to be treated:

1.2.1.1 The likelihood of death is great if the course of the condition is not halted.

1.2.1.2 The disease or condition causes irreversible morbidity

1.2.2 The situation for which a HUD may be appropriately applied shall exhibit all the following characteristics:

1.2.2.1 The situation necessitates the use of the investigational article;

1.2.2.2 No standard acceptable treatment is available;

1.2.2.3 There is insufficient time to seek IRB approval.
1.2.3. Except under certain circumstances investigators will seek informed consent from the prospective participant or their representative. Such consent will adhere as much as possible to that outlined by 21 CFR 50.

1.2.4. In obtaining informed consent from the prospective participant the investigator shall appropriately document such consent in accordance with 21 CFR 50.27.

1.2.5. If obtaining informed consent from the participant or the legally authorized representative is not feasible, the investigator and an independent physician (one who is not participating in the clinical investigation) must both certify that consent is not feasible and that the use of the test article is appropriate [21 CFR 50.23 (c)].

1.2.6. If time is not sufficient to obtain a determination by an independent physician, the investigator must provide certification in writing that the investigator, prior to the application of emergency use, determined that such consent was not feasible.

1.2.7. After the application of emergency use of a test article in which prior informed consent is not obtained, the investigator must submit to the IRB the written opinion of a physician not otherwise participating in the clinical investigation as to the accuracy of investigator’s judgment on the advisability of the emergency use and the investigator’s justification for not obtaining the participant’s informed consent.

IRB approval is for approval of the exemption from informed consent. It does not connote approval of the device itself. Approval of the emergency use of a test article is for one time only. Any subsequent use of the investigational product at the institution will have prospective IRB review and approval.

1.3 Objective

1.4 Responsibility

1.4.1. The Vice President for Research is ultimately responsible for this policy. Enabling parties include the Research Director of Research Compliance, the Chair of the Medical IRB, the Associate Dean for Research of the Medical School (CCHS?), and principal investigators.

1.4.2. The Director of Research Compliance and IRB Chair must provide appropriate forms on a timely basis and provide appropriate education regarding emergency use of a test article so that investigators are prepared and knowledgeable regarding such use.

1.4.3. Investigators are responsible for obtaining informed consent from participants or their representatives, obtaining physician opinion and documentation, and insuring that appropriate descriptions and other documentation pertinent to the application of emergency use are supplied to the IRB in a timely manner.

2.0 Procedure
2.1 Investigators will obtain, if feasible, the prospective participant's informed consent before the application of emergency use and document that consent.

2.2 If the prospective participant's informed consent is not obtainable, the investigator will seek that of a legally authorized representative of the prospective participant and document that consent.

2.3 If consent from the prospective participant or the legally authorized representative was obtained but there was insufficient time for prior IRB review, the investigator should complete FORM: Notification to IRB of Emergency Use of a Test Article, Parts A-C, and submit it to the IRB within 5 working days of the use of the test article.

2.4 If informed consent is not feasible, the investigator must seek the consultation of a physician not otherwise participating in the clinical investigation. The investigator and the physician must agree and must document by certifying in writing, before application of emergency use, that all of the following are true:

2.4.1. The likelihood of death is great if the course of the condition is not halted.
2.4.2. The disease or condition causes irreversible morbidity
2.4.3. The situation necessitates the use of the investigational article
2.4.4. No standard acceptable treatment is available
2.4.5. Insufficient time exists to seek IRB approval

2.5 If neither informed consent nor consultation with a physician not otherwise participating in the clinical investigation are feasible prior to the need for emergency use of a test article, the investigator will document, before application of emergency use, that all the following are true:

2.5.1. The likelihood of death is great if the course of the condition is not halted.
2.5.2. The disease or condition causes irreversible morbidity
2.5.3. The situation necessitates the use of the investigational article
2.5.4. No standard acceptable treatment is available
2.5.5. Insufficient time exists to seek IRB approval

2.6 If informed consent is not obtained and a physician is not consulted prior to the application of emergency use the investigator will supply to the IRB the written opinion of a physician not otherwise participating in the clinical investigation regarding the application of emergency use. This opinion must be provided within 5 working days of the application of emergency use and must address the following:

2.6.1. The likelihood of death if the course of the condition is not halted.
2.6.2. The likelihood of irreversible morbidity from the disease or condition
2.6.3. The situational necessity for the use of the investigational article
2.6.4. Existence and availability of standard acceptable treatment for the condition or disease

2.7 Informed consent is not required because all of the following are true:

2.7.1. Before the use of the test article both the investigator and a physician who is otherwise participating in the clinical investigation certified in writing that:
2.7.2. The participant is confronted by a life-threatening situation necessitating the use of the test article.
2.7.3. Informed consent cannot be obtained from the participant because of an inability to communicate with, or obtain legally effective consent from, the participant.
2.7.4. Time is not sufficient to obtain consent from the participant’s legal representative.
2.7.5. There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the participant.
2.7.6. The above written certification is submitted to the IRB within five working days after the use of the test article.

2.8 Informed consent is not required because all of the following are true:
2.8.1. Immediate use of the test article is, in the investigator’s opinion, required to preserve the life of the participant.
2.8.2. Time is not sufficient to obtain the independent determination a physician who is not otherwise participating in the clinical investigation.
2.8.3. Before the use of the test article the investigator will certify in writing all the following:
   The participant is confronted by a life-threatening situation necessitating the use of the test article.
   Informed consent cannot be obtained from the participant because of an inability to communicate with, or obtain legally effective consent from, the participant.
   Time is not sufficient to obtain consent from the participant’s legal representative.
   There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the participant.
2.8.4. The above written certification will be submitted to the IRB within five workings after the use of the test article.
2.8.5. The DRC report of the emergency use of a test article will be reviewed by the DRC and the exception to the requirement to obtain consent to determine whether the circumstances met FDA regulations.

2.9 After the use of the test article a physician who is not otherwise participating in the clinical investigation will certify in writing within five working days after the use of the article all of the following:
2.9.1 The participant is confronted by a life-threatening situation necessitating the use of the test article.
2.9.2 Informed consent cannot be obtained from the participant because of an inability to communicate with or obtain legally effective consent from the participant.
2.9.3 Time is not sufficient to obtain consent from the participant’s legal representative.
2.9.4 There is available no alternative method of or generally recognized therapy that provides an equal or greater likelihood of saving the life of the participant.

2.10 Investigators will notify IRB of the use of the test article, the investigator’s certification of the need for the use and the presence or absence of consent, and the independent physician’s opinion, whether before or after use of the device, using FORM: Notification to IRB of Emergency Use of a Test Article. The completed form should be submitted to the IRB Chair within five working days of the use of the article.
2.11 The IRB Chair or a designated member will review the notification form requesting exemption using FORM: Exemption from IRB Review for Emergency Use of a Test Article.

2.12 The Research Compliance Specialist will notify the investigator of the reviewer’s decision in writing. (No template letter was developed as the event is expected to be rare and the circumstances highly individual.)

3.0 REFERENCES

3.1 45 CFR §46 Waiver of Informed Consent Requirements in Certain Emergency Research (Federal Register, Vol. 61, No. 192, pp 51531-51533, October 2, 1996).

3.2 45 CFR §46.116 (f)

3.3 21 CFR §56.102 (d)

3.4 21 CFR §56.104(c)

3.5 FDA: Information Sheets—Exception from Informed Consent for Studies Conducted in Emergency Settings

3.6 DoD: DoDD 3216.2, para 4.2’ SECNAVINST 3900.39D, para. 6a(3) and 7a(1); wo U.S.C., 980 (a,b).

4.0 RELATED SECTIONS

4.1 FORM: Notification to IRB of Emergency Use of a Test Article

4.2 FORM: Exemption from IRB Review for Emergency Use of a Test Article