

Policy and Procedure

	ENTITY/HOSPITAL	NUMBER
	INTEGRIS Health	SYS-RES-103
	MANUAL	EFFECTIVE DATE
	System Policies	3/16
	SUBJECT	REVISED
	IRB EMERGENCY USE	

1.0 PURPOSE

The purpose of this IRB Emergency Use Policy (“Policy”) is to set forth requirements for Emergency Use of a test article on a human subject and to outline the responsibilities of the physician/investigator when requesting Emergency Use at any INTEGRIS Health facility (“INTEGRIS”).

2.0 POLICY

This Policy outlines the responsibilities of the physician when an emergency requires that a patient be treated with a Test Article such that there is not sufficient time to obtain Institutional Review Board (“IRB”) review and approval at a convened meeting. This is an exception to the general rule that Test Articles may only be used in human subjects who are participating in a clinical investigation/research. Emergency Uses are for the purpose of providing clinical treatment and are not considered to be research according to OHRP regulations at 45 CFR 46.102(d). Whenever possible, informed consent should be obtained before the Test Article is used. Emergency Uses are exempt from the requirement to obtain prior IRB review and approval, provided that the use is reported to the IRB within five (5) working days after initiation of the Emergency Use. 21 CFR 56.104(c). The physician should complete as many of the patient protection measures detailed in this policy as possible before using the Test Article. If a physician anticipates using a Test Article more than one time at INTEGRIS, the physician should contact the IRB about the need to submit an IRB application for prospective IRB review and approval of a research study.

3.0 SCOPE

This Policy applies to all organizations within INTEGRIS Health, Inc., and all personnel of such entities.

4.0 DEFINITIONS

- 4.1 Emergency Use means 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.
- 4.2 Immediately Life-Threatening Disease or Condition means a stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.
- 4.3 Investigational New Drug Application (“IND”) means an FDA submission that requires permission to use an investigational drug/biologic in a patient. One type of IND is the “emergency IND,” which allows the FDA to authorize the use of an investigational drug/biologic in an emergency situation that does not allow time for prior submission of an IND application in accordance with FDA regulations. It is also used for patients who do not meet the criteria of an existing study protocol, or if an approved study protocol does not exist for the drug/biologic.
- 4.4 Investigational Device Exemption (“IDE”) means the request for FDA permission to use an investigational device in a patient. An “emergency IDE” may be needed when an IDE for the device does not exist; when a physician wants to use a device in a way not approved under

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an approved IDE; or when a physician is not an investigator under the relevant IDE (i.e., not participating in the clinical investigation of the device).

4.5 Life-Threatening Condition means serious diseases or conditions such as sight-threatening and limb-threatening conditions as well as other situations involving risk of irreversible morbidity (e.g., blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke). FDA Device Guidance.

4.6 Serious Disease or Condition means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is a serious matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. 21 CFR 312.300(b)

4.7 Test Article means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to FDA regulation. 21 CFR 56.102(l)

5.0 PROCEDURE

5.1 Determination of Appropriateness of Emergency Use

5.1.1 Drugs/Biologics The physician shall determine if the following are met:

5.1.1.1 The patient is suffering from an Immediately Life-Threatening Disease or Condition or a Serious Disease or Condition that needs immediate treatment;

5.1.1.2 There is no generally acceptable alternative for treating the patient available;

5.1.1.3 Due to the immediate need to use the Test Article, there is no time to follow existing policies and procedures to obtain IRB approval prior to the use; and

5.1.1.4 The physician shall determine if the probable risk to the person from the investigational Test Article is not greater than the probable risk from the disease or condition. 21 CFR 312.310(a)(1)

The physician must then provide information to the FDA, so that the following determinations may be made:

5.1.1.5 The patient to be treated has an Immediately Life-Threatening Disease or Condition or a Serious Disease or Condition, and there is no

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comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;

- 5.1.1.6 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;
- 5.1.1.7 Providing the investigational test article 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; and
- 5.1.1.8 The patient cannot obtain the Test Article under another IND or protocol.
- 5.1.2 Devices The physician shall determine if the following requirements are met:
 - 5.1.2.1 The patient has a Life-Threatening Condition that needs immediate treatment;
 - 5.1.2.2 No generally acceptable alternative treatment for the condition exists;
 - 5.1.2.3 Because of the immediate need to use the device, there is no time to follow existing policies and procedures to get IRB and FDA approval for the use; and
 - 5.1.2.4 The physician shall assess the potential for benefit from the use of the unapproved device, and determine that there is a substantial reason to believe that benefits will exist.

The physician must obtain the determination of an uninvolved physician (one not participating in the Emergency Use) to determine that all of the above Emergency Use criteria are met and must:

 - 5.1.2.5 Obtain documentation of the uninvolved physician’s determination whenever possible (usually via email), and
 - 5.1.2.6 If it is not possible to obtain a second opinion from an uninvolved physician (and/or documentation), the treating physician should make the determination and proceed with the Emergency Use process.

5.2 Obtaining the Test Article

- 5.2.1 Drugs/Biologics – IND The physician must take the following steps to obtain the Test Article:
 - 5.2.1.1 Identify the Sponsor

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- (a) If the manufacturer of the drug/device has an IND, then the manufacturer shall serve as the sponsor of the Emergency Use.
- (b) If the manufacturer does not have any plans to get an IND, then the physician shall serve as the “sponsor investigator” of the Emergency Use.

5.2.1.2 Contact the Sponsor to determine whether they are willing to provide the investigational drug/biologic.

5.2.1.3 Contact the FDA for an Emergency IND

- (a) If the manufacturer will serve as the sponsor, manufacturer/sponsor will usually contact the FDA on the physician’s behalf for approval of an emergency IND.
- (b) If the physician will serve as the “sponsor,” the physician, or the physician’s designee, contacts the FDA directly to obtain an emergency IND. An Emergency Use may be requested by telephone, facsimile, email, or other means of electronic communication.
- (c) The physician or sponsor must explain how the expanded access use will meet the above criteria for emergency use.
- (d) The FDA will provide a new IND number for the specific Emergency Use.

5.2.2 Devices – IDE The physician must take the following steps to obtain the Test Article:

5.2.2.1 Identify the sponsor, which will generally be a manufacturer who has applied for an IDE and will serve as the “sponsor” of the Emergency Use.

5.2.2.2 Contact the sponsor to determine whether they are willing to provide the investigational device.

For devices, prior FDA approval for shipment or Emergency Use of an investigational device is not required. 21 CFR 812.35(a)(2) Treating physician may contact the Office of Device Evaluation (ODE) at FDA to discuss his/her patient’s condition. In this situation, ODE acts in an advisory role. The responsibility for making the decision as to whether the situation meets the Emergency Use criteria and whether the investigational device should be used lies with the treating physician.

If no IDE exists, the physician should follow the above procedures and report the Emergency Use to CDRH as directed in Section 5.5.

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5.3 Patient Protection Measures Patient care should not be compromised in the event there is insufficient time to complete all of these measures:

5.3.1 Concurrence of the IRB Office and the IRB Chair or Designee (the Director of Research and Grants)

5.3.1.1 The physician shall email the Emergency Use Report Form (see **Attachment 1**) to the IRB Office (IRB@integrisok.com) and the IRB Chair or Designee before calling, if possible, so the IRB Office, the IRB Chair or Designee can reference the Form during the call.

5.3.1.2 Once the physician has emailed the Emergency Use Report Form the physician will call the IRB Office and the IRB Chair or Designee to consult regarding the Emergency Use request.

5.3.1.3 The IRB Office will send a confirmation letter to the physician once it has been determined by the IRB Office and the IRB Chair (or Designee) that the Emergency Use is appropriate.

5.3.2 Written Informed Consent Since the FDA exempts Emergency Use from the usual requirements for prior IRB approval, there is not a requirement to obtain IRB approval of the Emergency Use consent for before using it with the patient. However, this Policy contemplates that the consent form should be reviewed and approved by the IRB Office and INTEGRIS Legal Services.

OR

If it is not possible to obtain consent, FDA regulations (21 CFR 50.23) allow a waiver of Emergency Use consent under the following conditions:

5.3.2.1 The patient is confronted with a life-threatening situation necessitating the use of the Test Article;

5.3.2.2 Informed Consent cannot be obtained from the patient because of an inability to communicate with, or obtain legally effective consent from, the patient;

5.3.2.3 Time is not sufficient to obtain consent from the patient's legal representative; and

5.3.2.4 No alternative method of approved or generally recognized therapy is available that provides equal or greater likelihood of saving the patient's life.

5.3.3 Independent Physician Determination If immediate use of the Test Article is needed to preserve the patient's life, and there is not sufficient time to secure an independent physician's determination that the four conditions for a waiver of

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Emergency Use consent (described above in Section 5.3.2) apply, the treating physician should make the determination that consent cannot be obtained and proceed, but must have his/her written determination reviewed in writing by an independent physician within five working days after the Emergency Use of the Test Article. 21 CFR 50.23(b) and (c); 21 CFR 812.150(a)(5).

5.3.4 Devices Only As noted above in Section 5.1.2, obtain a written assessment from an uninvolved physician that the criteria for Emergency Use (this is not referring to waiving consent) are satisfied for the patient.

5.3.5 Devices Only As noted in Section 5.2.2, obtain authorization from the IDE sponsor if an approved IDE exists for the device.

5.4 Initiate Treatment with the Test Article

5.4.1 Initiate Use of the Drug/Biologic (IND) Treatment may begin when the Emergency Use is authorized by the FDA reviewing official. 21 CFR 312.305(d)(2)(i).

5.4.2 Initiate Use of the Device (IDE). Emergency Use of the device may begin when the use is authorized by the IDE sponsor.

5.5 Submit a Follow-up Report to the IRB A follow-up report **must** be submitted to the IRB within five (5) working days of the initiation of treatment. Physician shall complete the remaining sections of the Emergency Use Report Form, sign and date, and send to the IRB Office and the IRB Chair (or Designee) within five (5) working days after initiation of the Emergency Use. In addition to completing the Emergency Use Report, the following must be met, if applicable:

5.5.1 Reports for Drugs/Biologics (IND) Physician must also submit an expanded access submission to the FDA within fifteen (15) working days of the FDA's authorization of the Emergency Use. 21 CFR 312.310(d)(2). See Form FDA 1571 and Instructions.

5.5.2 Reports for Devices (IDE) An investigator shall notify the IDE sponsor (who will notify the FDA) of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but in no event later than five (5) working days after the emergency use occurred. 21 CFR 812.35(a)(2); 21 CFR 812.150(a)(4).

5.5.2.1 The report should contain a summary of the conditions constituting the emergency, the patient protection measures that were followed, and patient outcome information.

5.5.2.2 If no IDE exists, the physician should follow the above procedures and report the emergency use to CDRH or CBER.

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5.5.2.3 Informed consent: If an investigator uses a device without obtaining informed consent, the investigator shall report such use to the sponsor and the reviewing IRB within five (5) working days after the use occurs. 21 CFR 812.150(a)(5).

5.6 Convened IRB Follow-Up Report

5.6.1 The physician shall complete Section G. of the Emergency Use Report Form and submit to the IRB for review. The physician must document the following on the Emergency Use Report Form:

- 5.6.1.1 Date of Completion of Treatment
- 5.6.1.2 Whether there was an indefinite use of the treatment (i.e., on-going use of a drug/biologic or device)
- 5.6.1.3 Status of Patient upon Completion of Treatment
- 5.6.1.4 Outcome of Treatment
- 5.6.1.5 Any Adverse Effects of Treatment

If there was indefinite use, the physician must submit a continuing review report of the indefinite Emergency Use to the convened IRB at six (6) months, one year, and annually thereafter until either completion of the treatment or approval by the FDA.

- 5.6.2 The IRB will review whether the situation satisfied the Emergency Use criteria, whether the physician followed reasonable patient protection measures under the circumstances, the patient outcome information, and whether future uses of the Test Article are anticipated such that an application should be submitted to the IRB. Such review shall occur at a meeting of the convened full IRB.
- 5.6.3 Subsequent Emergency Uses of the Test Article for the same indication should not occur unless the physician or another physician obtains FDA and IRB approval for the drug/biologic/device and its use. (FDA acknowledges that it would be inappropriate to deny emergency treatment to a second patient if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the application.)
- 5.6.4 If an IND or IDE application for subsequent use has been filed with FDA and FDA disapproves the application, the drug/biologic/device may not be used even if the circumstances constituting an emergency exist.

5.7 IRB Correspondence The IRB will provide correspondence to the physician in the form of an outcome letter either confirming that all regulatory requirements have been satisfied, or will highlight deficiencies and request additional actions.