ORLANDO HEALTH®

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Type of Policy:	***PROTECTION OF HUMAN RESEARCH PARTICIPANTS***	Category:	**Orlando Health Institutional Review Board (IRB)**

Title:	***Compassionate Use /Treatment Use/Expanded Access of an Investigational Drug or Device***	Policy #:	**0330-1012**
		Replaced #:	ORMC IRB# 6000-200 MDACCO IRB# 1000-0001
Page 1 of 5		Issued By:	Orlando Health Institutional Review Board (IRB)
Issue Date:	**4/1/04**	Approved By:	Mildred Beam, Esq. Orlando Health, Inc. Institutional Official **SIGNATURE ON FILE**
Revision Dates:	5/14/04, 11/23/07, 9/23/13, 6/1/15, 3/26/18		

I. PURPOSE:

This policy outlines the process for compassionate/treatment use of investigational drugs and devices.

II. DEFINITIONS:

A. Test article means an investigational drug or device not approved by FDA.

B. Life-Threatening for the purposes of Code of Federal Regulations section 56.102(d) includes the scope of both life-threatening and severely debilitating, as defined below:

1. Life-threatening means diseases or conditions 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. The criteria for life-threatening do 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 in which no standard treatment is available requiring intervention before review at a convened meeting of the IRB is feasible.
2. Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

III. POLICY:

It is Orlando Health IRB's policy that compassionate/treatment use of an investigational drug or device shall be done only in accordance with federal regulations.

IV. PROCEDURES

IVa. IRB PROCESSING OF A REQUEST FOR "COMPASSIONATE USE" OF AN INVESTIGATIONAL DEVICE:

A. FDA recognizes that there are circumstances in which an investigational device is the only option available for a patient faced with a serious, albeit not life-threatening condition. FDA concurrence/approval is needed before compassionate use occurs. **Compassionate use of an unapproved device is intended for an individual patient or small group of patients and does not constitute human subjects research.**

B. Under compassionate use, a physician can use an unapproved device to treat, diagnose or monitor a patient with a serious disease or condition.

C. Responsibilities of the treating physician:

1. Request authorization to obtain the investigational device from the sponsor. The sponsor may agree or disagree. If the sponsor disagrees, the physician cannot use the device.

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2. Devise a schedule for patient monitoring taking into consideration the investigational nature of the device, to address the specific needs of the patient, and to detect any possible problems with the use of the device.
3. Obtain FDA's concurrence/approval for the "compassionate use".
4. Obtain clearance from the institution, if appropriate.
5. Obtain an independent assessment from an uninvolved physician.
6. Submit the "Compassionate Use of an Investigational Device" Submission Form with its supporting documentation and obtain the IRB Chairperson's or Vice Chairperson's concurrence.
7. Obtain informed consent from the patient using an IRB-approved consent form on the Orlando Health template.
8. Report any problems from the use of the device to the IRB and the sponsor as soon as possible.
9. Write a follow-up summary of the compassionate use and provide it to the sponsor. Submit a continuing review report with the follow-up summary to the IRB per IRB instructions, at least once a year.

D. Sponsor responsibilities: If the sponsor disagrees with the use, the physician cannot use the investigational device for compassionate use. If the sponsor agrees with the use, an IDE supplement is submitted to the FDA requesting approval for a compassionate use under 21 CFR 812.35(a) in order to treat the patient. The IDE supplement should include the following:

- A description of the patient's condition and the circumstances necessitating treatment
- A discussion of why alternative therapies are unsatisfactory and why the probable risk of using the investigational device is not greater than the probable risk from the disease or condition
- An identification of any deviations in the approved clinical protocol that may be needed in order to treat the patient.
- The patient protection measures that will be followed (informed consent, concurrence of IRB chairperson, clearance from the institution, independent assessment from uninvolved physician, authorization from sponsor).

E. IRB responsibilities:

1. The IRB Chairperson or Vice-chairperson shall determine whether they concur with the compassionate use request and that it fulfills all of the following FDA criteria:
   - No standard acceptable treatment is available, and
   - The device is not yet approved for the serious disease or condition, and
   - The patient does not meet entry criteria for ongoing research studies.
2. The IRB must:
   - Document concurrence of the IRB Chairperson or Vice-chairperson
   - Ensure FDA concurrence/approval for the compassionate use

- Review and approve the informed consent document prior to use
- Receive reports of any problems with the use
- Receive follow-up reports after the use

IVb. IRB PROCESSING FOR TREATMENT USE OF A DEVICE:

A. "Treatment Use" is described in the federal regulations to facilitate broader availability of promising new therapies to desperately ill patients as early in the development process as possible (for example, before general marketing begins, or to obtain additional data on the device's safety and effectiveness). Under these regulations, these procedures apply to patients faced with a serious or life-threatening disease/condition for which no alternative exists.

B. Under the federal regulations, treatment use of an investigational device will be considered when:

1. The device is intended to treat or diagnose a serious or immediately life-threatening disease or condition;
2. There is no alternative device available to treat or diagnose the disease or condition in the intended patient population;
3. The device is under investigation in a controlled clinical trial for the same use under an approved IDE, or all clinical trials have been completed; and
4. The sponsor of the controlled clinical trial is pursuing marketing approval/clearance of the investigational device with due diligence.

C. If above conditions are met, the Principal Investigator, either through the sponsor or directly with the FDA, must obtain a Treatment Use IDE. The Principal Investigator would then submit a new protocol application to the IRB following procedures outlined in IRB Policy #0330-1014 "New/Initial Protocol Submission/Full Board Review"

D. For **Emergency Use of an Investigational Device**, see IRB policy #0330-1010 "Emergency Use of Investigational Drugs and Devices".

IVc. IRB PROCESSING FOR TREATMENT USE OF INVESTIGATIONAL DRUGS

A. Open Label protocol or Open Protocol IND: These are usually uncontrolled studies, carried out to obtain additional safety data (Phase 3 studies). They are typically used when the controlled trial has ended and treatment is continued so that the subjects and the controls may continue to receive the benefits of the investigational drug until marketing approval is obtained. These studies require prospective Institutional Review Board (IRB) review and informed consent.

B. Treatment IND: The treatment IND [21 CFR 312.34 and 312.35] is a mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. A treatment IND may be granted after sufficient data have been collected to

show that the drug "may be effective" and does not have unreasonable risks. Because data related to safety and side effects are collected, treatment INDs also serve to expand the body of knowledge about the drug.

There are four requirements that must be met before a treatment IND can be issued:

- The drug is intended to treat a serious or immediately life-threatening disease;
- There is no satisfactory alternative treatment available;
- The drug is already under investigation, or trials have been completed; and
- The trial sponsor is actively pursuing marketing approval.

Treatment IND studies require prospective IRB review and informed consent.

Treatment INDs are discussed under the general heading of expanded access to investigational drugs. On August 13, 2009, FDA issued in the Federal Register 21 CFR Part 312 and 316, "Charging for Investigational Drugs Under and Investigational New Drug Application; Expanded Access to Investigational Drugs for Treatment Use; Final Rules". These rules and the accompanying preamble are available at http://edocket.access.gpo.gov/2009/pdf/E9-19004.pdf

C. Group C Treatment IND: The "Group C" treatment IND was established by agreement between the FDA and the National Cancer Institute (NCI). The Group C program is a means for the distribution of investigational agents to oncologists for the treatment of cancer under protocols outside the controlled clinical trial. Group C drugs are generally Phase 3 study drugs that have shown evidence of relative and reproducible efficacy in a specific tumor type. They can generally be administered by properly trained physicians without the need for specialized supportive care facilities. Group C drugs are distributed only by the national Institutes of Health under NCI protocols. Although treatment is the primary objective and patients treated under Group C guidelines are not part of a clinical trial, safety and effectiveness data are collected.

D. Parallel Track: Persons with AIDS or HIV-related diseases who are not able to take standard therapy or for whom standard therapy is no longer effective, and are not able to participate in controlled clinical trials, may have access to new IND drugs via parallel track. These patients may receive these drugs in studies without concurrent control groups while parallel studies that use controlled investigations are underway. Parallel track is similar to treatment IND, but less evidence of effectiveness is required. Applications for parallel track therapies must be made to the FDA, and require IRB approval and informed consent.

E. Emergency Use IND: The need for an investigational drug may arise in an emergency situation that does not allow time for submission of an IND in the usual manner. See IRB policy #0330-1010 "Emergency Use of Investigational Drugs and Devices".

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- **Individual (Single) Patient IND:** When a physician would like to submit an Investigational New Drug application (IND) to obtain an unapproved drug for an individual patient, he or she should first ensure that the manufacturer of the unapproved drug is willing to provide the drug. If the manufacturer agrees to provide the drug, the physician should submit an IND to the appropriate review division. A copy of the FDA individual patient IND submission packet (including FDA Form 3926) and the FDA response including the IND number assigned must be sent to the IRB for approval prior to use of the drug.

In an emergency situation, the request to use the drug may be made via telephone or other rapid means of communication, and authorization to ship and use the drug may be given by the FDA official over the telephone. In these situations, known as emergency INDs, shipment of and treatment with the drug may begin prior to FDA's receipt of the written IND submission that is to follow the initial request. Please refer to IRB policy #0330-1010 "Emergency Use of Investigational Drugs and Devices". A copy of the FDA individual patient IND submission packet and the IND number assigned by the FDA must be sent to the IRB for acknowledgement within 5 calendar days of use of the drug.

Once treatment has begun the following must be reported to the IRB:

1) All Serious Adverse Events should be reported. Please refer to IRB policy #0330-1000 "Reporting Serious Adverse Events".
2) Annual continuing review (see IRB Policy #0330-1007 "Continuing Review Process") of the IND must be submitted including the Emergency Use Progress Report describing the patient's status.
3) Termination of the use of the drug

IVd. <u>DOCUMENTATION:</u>

A. In addition to documentation required in IRB Policy #0330-1014 "New Protocol Submission", the IRB file will contain the Treatment Use IND/IDE number from the FDA.
B. IRB Actions shall be documented in the IRB meeting minutes.

V. <u>REFERENCES</u>:

A. Code of Federal Regulations – 21 CFR 812.35(a), 21 CFR 56.104(c), 21 CFR 56.102(d), 21 CFR 56.108(a)(3), 21 CFR 312.34 and 312.35, 21 CFR Part 312 and 316,
B. Federal Register: 57 FR 13250
C. http://www.fda.gov/downloads/Training/CDRHLearn/UCM180888.pdf

VI. <u>ATTACHMENTS:</u>

None