7 Investigational Drugs & Devices in Research

7.1 Investigational Drug Policy

All Investigational Drugs, Agents and/or Biologics used in Human Subjects Research under the purview of Tulane’s IRB shall be stored, handled, and dispensed in compliance with regulations or requirements of the FDA, the Louisiana State Board of Pharmacy (“LSBP”), The Joint Commission, Federal, State and other laws and regulations, and the policies and procedures of the HRPP. Furthermore, if Research is conducted on hospital premises, such Research shall be conducted in accordance with applicable hospital and medical staff polices and guidelines.

The University is affiliated with and routinely conducts Human Subjects Research at Tulane University Hospital and Clinic (“TUHC”), which may require the provision of clinical care to Research subjects in a hospital setting. To this end, TUHC serves as a primary site for hospital-based clinical Research conducted by the University. For this reason, the University and TUHC entered into a Master Clinical Trial Affiliation Agreement (“Master CTA Agreement”) to facilitate the provision of necessary Research-support services, supplies and equipment, and the use of TUHC facilities including, without limitation, TUHC pharmacy services. The Master CTA Agreement only applies to Research conducted at TUHC’s Downtown and Lakeside campuses, as well as any Institution ambulatory clinic (i.e., outpatient) physically located within them (“TUHC Facility”).

TUHC’s Department of Pharmacy (“TUHC Research Pharmacy”) provides administrative and clinical services to PIs, Investigators and Research staff involved in Drug-related Research conducted at TUHC’s Facility under the purview of Tulane’s IRB. Furthermore, a TUHC research pharmacist (“Research Pharmacist”) will serve as a member on the Biomedical IRB to allow TUHC Research Pharmacy to have complete information about all IRB-approved Research that takes place at the TUHC’s Facility. Inclusion of the Research Pharmacist as an IRB member assures that information about all studies involving Drugs used in Research is shared with both the TUHC Research Pharmacy staff as appropriate and that TUHC’s Pharmacy and Therapeutics Committee is made aware of IRB-approved Research involving Drugs.

Regardless of whether Investigators conduct Investigational Drug studies for inpatients or outpatients, the Institution’s policy requires that the IRB review and approve all Investigational Drug Research involving Human Subjects prior to initiation of the study and prior to enrollment of subjects.

Institutional policy requires the Research Pharmacist to provide advice to the IRB with respect to all activities relating to the distribution, storage, dispensing, and accountability for Investigational Drug products for use in Human Subjects.


7.2 Definitions

Administer (or “Administration” or “Administering”): Means the direct application of a Drug to the body of a patient or Research subject by injecting, inhalation, ingestion, or any other means. [LA R.S. 37:1164].
**Agent(s):** are chemical agents that affect the function of living things.

**Biologic:** a substance made from a living organism or its products and used in the prevention, diagnosis, or treatment of certain health conditions.

**Biological Products:** are a subset of Drugs used for the treatment, prevention or cure of disease in humans. FDA regulations and policies have established that Biological Products include blood-derived products, vaccines, *in vivo* diagnostic allergenic products, immunoglobulin products, products containing cells or microorganisms, and most protein products. Biological Products, like other Drugs, can be studied in clinical trials involving Humans Subjects under an IND in accordance with the regulations at 21 CFR §312.

**Clinical Investigation:** means any experiment that involves a Test Article and one or more Human Subjects and that either is subject to requirements for prior submission to the FDA under section 505 of the Federal Food, Drug, and Cosmetic Act (the “FDA Act”) [21 U.S.C. §355] or to, or held for inspection by the Food and Drug Administration (“FDA”) as part of an application for a Research or marketing permit. [21 CFR §50.3]

**Dispense (or Dispensing):** means the interpretation, evaluation, and implementation of a prescription Drug order, including the preparation and delivery of a Drug or Device to a patient or patient's agent in a suitable container appropriately labeled for subsequent administration to, or use by, a patient. “Dispense” necessarily includes a transfer of possession of a Drug or Device to the patient or the patient's agent. [LA R.S. 37:1164]. Louisiana law requires that Dispensing may only be done by a licensed pharmacist or a physician who is registered with the board as a dispensing physician. [LA R.S. 37:1201].

**Distribute (or Distribution):** means the delivery of a Drug or Device other than by Administering or Dispensing.

**Drug:** means: (a) any substance recognized in the official compendium, or supplement thereto, designated by the Louisiana Board of Pharmacy (or other appropriate jurisdiction) for use in the diagnosis, cure, mitigation, treatment or prevention of diseases in humans, (b) any substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans, or (c) any substance other than food intended to affect the structure or any function of the body of humans. [LA-R.S. 37:1164].

**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. [FDA 21 CFR §56.102(d)]. This is not to be confused with Planned Emergency Research.

**Investigational Drug (or “Investigational New Drug”):** means a new Drug or Biological that is used in Research. It also includes a Biologic used *in vitro* for diagnostic purposes. The FDA considers the term “Investigational New Drug” or “Investigational Drug” to be synonymous with Investigational Drug. [FDA 21 CFR §312.2]. However, for purposes of this document, an Investigational Drug includes the following:

- An approved Drug that is being studied for an unapproved or approved use in a controlled, randomized or Blinded clinical trial.
Those new Drugs for which the PI or a Sponsor has filed an IND application [FDA 21 CFR §312] which are exempt from pre-marketing approval requirements and may be lawfully shipped for use in Clinical Investigations in Human Subjects.

A Drug that is lawfully marketed in the U.S. that may still be considered investigational and required that an IND be filed if the proposed use of such a Drug involves a controlled study aimed towards seeking a significant change in labeling, advertising, route of Administration, dosage level, or other factor that affects the risks associated with the use of the product. [FDA 21 CFR §312.3(b)].

**Investigational Drug Application (or “IND”):** refers to either an Investigational New Drug application or to a new Drug that is used in Clinical Investigations. IND is synonymous with “Notice of Claimed Investigational Exemption for a New Drug.” [FDA 21 CFR §312].

**Planned Emergency Research:** is the conduct of planned Research in life threatening emergencies where the requirement to obtain prospective informed consent has been waived. [21 CFR §50.24]. The Research plan must be approved in advance by the FDA or DHHS and the IRB, and publicly disclosed to the community in which the Research will be conducted. This term should not to be confused with Emergency Use.

**Test Article:** is any Drug (including a Biological for human use), medical device for Human use, human additive, color additive, electronic product, or any other article subject to FDA regulation. [FDA 21 CFR §50.3(j); 21 CFR §56.102(l)].

### 7.3 FDA Exemptions

The following categories of Clinical Investigations are Exempt from the requirements of FDA regulations for IRB review:

1. Emergency Use of a Test Article, provided that such Emergency Use is reported to the IRB within 5 working days. Any subsequent use of the Test Article at the Institution is subject to IRB review. [FDA 21 CFR §56.104(c)].

2. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or approved by the EPA or the Food Safety and Inspection Service of the U.S. DOA. [FDA 21 CFR §56.104(d)].

### 7.4 IND Requirements

The PI must indicate on the **IRB Application** (TU Form 102) whether the Research involves Investigational Drugs. If so, the PI must indicate if there is an IND for the Research and provide documented assurance from the Sponsor that the manufacture and formulation of investigational or unlicensed Test Articles conform to Federal regulations. Documentation of the IND could be:

1. Industry sponsored Protocol with IND.

2. Letter from FDA.

3. Letter from industry Sponsor.

4. Other document and/or communication verifying the IND.
If the Research involves Drugs and there is no IND, the PI must provide a rationale why it is not required.

The IRB will review the application and determine:

1. Whether there is an IND and if so, whether there is appropriate supporting documentation.
2. If the Research involves Drugs or Devices with no IND, and whether the Research meets the criteria below.

7.4.1 IND Exemption

For Drugs, an IND is not necessary if all seven of the following conditions are met:

1. The Drug being used in the Research is lawfully marketed in the U.S.;
2. The Research is not intended to be reported to FDA in support of a new indication for use or to support any other significant change in the labeling for the Drug;
3. The Research is not intended to support a significant change in the advertising for the product;
4. The Research does not involve a route of Administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the Drug product;
5. The Research is conducted in compliance with the requirements for IRB review and informed consent [FDA 21 CFR parts 56 and 50];
6. The Research is conducted in compliance with the requirements concerning the promotion and sale of Drugs [FDA 21 CFR §312.7];
7. The Research does not intend to invoke 21 CFR §50.24 (Exception from informed consent requirements for emergency Research).

Note: The following are also Exempt from the IND requirements: (a) a Clinical Investigation involving use of a placebo if the investigation does not otherwise require submission of an IND; and (b) a Drug intended solely for tests in vitro or in laboratory Research animals if shipped in accordance with 21 CFR §312.160.

For Clinical Investigations involving an in vitro diagnostic Biological Product, anIND is not necessary if:

1. It involves one or more of the following: (a) Blood grouping serum, (b) Reagent red blood cells or (c) Anti-human globulin;
2. It is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and
3. It is shipped in compliance with 21 CFR 312.160.

7.4.2 Responsibilities

This Section describes the responsibilities and related responsibilities for handling Investigational Drugs or unlicensed Test Articles with respect to pharmacy, inventory control, reporting and documentation.
Regulations & Guidelines: FDA 21 CFR §312.61; 21 CFR §312.62; 21 CFR §312.69; AAHRPP I.5.B.

7.4.2.1 Principal Investigator

The PI is responsible for ensuring that the Research is conducted according to all regulatory guidelines and University policies and procedures. PIs should refer to the Guidance on Special Considerations & Reporting Requirements for FDA- and NIH-Regulated Items (TU Form 711) found on HRPO’s Website for additional assistance.

For TUHC inpatients, Investigational Drugs for inpatient Research studies must be dispensed by TUHC Research Pharmacy. For outpatients at a TUHC Facility and/or at a non-TUHC Facility, only a licensed pharmacist can dispense Investigational Drugs. Typically, this can take place at a retail pharmacy, or TUHC’s outpatient pharmacy. Where a PI requests to have control of the Investigational Drug, Agent or Biologic with respect to outpatients in a non-TUHC Facility, then the PI must submit for IRB approval a plan for the distribution, storage, dispensing, and accountability for the Investigational Drug product(s). Such plan must involve the PI contracting with a pharmacist such that the pharmacist is responsible for dispensing.

1. Dispensing to Inpatients—TUHC Research Pharmacy Coordination: For hospital inpatients, the PI must use TUHC Research Pharmacy (or equivalent at other non-TUHC hospital) as the coordinating and control center for the Research Drug. As the coordinating and control center, TUHC Research Pharmacy assumes the responsibility for maintaining records of the Drugs delivered to the TUHC Research Pharmacy, inventory of the Drug, dispensing of Drugs to Research subjects, and then return to the Sponsor or disposition of unused product. TUHC Research Pharmacy will store and dispense the Investigational Drug as specified by the Sponsor and in accordance with applicable regulatory requirements.

TUHC Research Pharmacy may initiate or adjust Drug therapy and/or order laboratory tests associated with a Research Protocol when requested to do so by the PI. Any pharmacist participating in such a Protocol must be trained and deemed competent to participate by the PI (or his/her designee). Specific details on the adjustment of Drug therapy or ordering of laboratory tests should be reviewed during the Protocol initiation visit.

When TUHC Research Pharmacy is the coordinating and control center for the Research Drug, TUHC Research Pharmacy will store the returned dispensed Investigational Drug in a designated return area when a study Protocol requires the subject to return the empty Investigational Drug container or any amount of the unused Investigational Drug. However, it is the responsibility of the PI to deliver the returned dispensed Investigational Drug to Research Pharmacy when subjects leave the dispensed Investigational Drug in the PI’s department.

When TUHC Research Pharmacy is coordinating the control of the Research Drug, the PI will forward a copy of the complete Research Protocol, a copy of the Investigator’s Drug brochure, ordering procedures, any special storage, handling or preparation requirements, and any pertinent dispensing information to the Research pharmacist.

A cost estimate should be obtained from TUHC Research Pharmacy during the initial stages of budget development. The mandatory Institutional pharmacy fee will be applied.
to all Research involving Investigational Drugs. TUHC Research Pharmacy will prepare a cost estimate of other pharmacy fees after review of the above material. The PI should provide TUHC Research Pharmacy with the account number to which any supplies should be billed. For further information please refer to Tulane Department of Pharmacy Policies.

Regulations & Guidelines: AAHRPP I.2.D.

2. **Dispensing Controlled Substances**: Controlled substances must be securely stored and must be administered by a duly licensed pharmacist.

3. **Dispensing to Outpatients**: Typically TUHC’s outpatient pharmacy (and rarely a retail outpatient pharmacy) is responsible for coordinating the control of and dispensing the investigational Drug. Dispensing of an Investigational Drug, Agent or Biologic by a PI with respect to Research Under the Auspices of Tulane’s IRB is not permitted.

When the PI (through a contracted pharmacist) retains control of Investigational Drug supplies, the PI shall ensure that the contracted pharmacist is responsible for ensuring that the Research is conducted according to all regulatory guidelines and Tulane policies and procedures, including but not limited to:

a. **Drug Accountability Record** - The PI (through the contracted pharmacist) must maintain records of the product’s delivery to the study site, the inventory at the site, the use by each subject, and the return to the Sponsor or alternative disposition of unused product. These records should include dates, quantities, batch/serial numbers, expiration dates, and the unique code numbers assigned to the investigational product(s) and trial subjects. The PI (through the contracted pharmacist) should maintain records that document adequately that the subjects will provide the doses specified by the Protocol and reconcile all investigational product(s) received from the Sponsor. The Investigational Drug supply is subject to audit by the IRB.

   In regard to the “use by each subject”, PIs (through the contracted pharmacist) should maintain Drug accountability records that document adequately which subject(s) received the Drug; when the subject(s) received the Drug; the specific dosage the subject(s) received; and any returned amount of the dispensed Investigational Drug;

b. **Drug Storage** – Investigational product(s) should be stored as specified by the Sponsor and in accordance with applicable regulatory requirement(s). Storage guidelines, include:

   i. Storage area is large enough for the supply of study Drug.
   ii. Storage area can be locked.
   iii. Investigational Drug is stored separately from other compounds.
   iv. Non-dispensed Drug is stored separately from returned dispensed Drug.

   - If the study Protocol requires the subject to return the empty Investigational Drug container or any amount of the unused Investigational Drug, it is the Investigators responsibility to store the returned dispensed Investigational Drug separately from the non-dispensed Investigational Drug.
• It is the responsibility of the PI to deliver the returned dispensed
  Investigational Drug to Research Pharmacy if it is the coordinating and
  control center for the Research Drug

v. Inventory control procedures are used.

vi. Any environmental controls are maintained.

vii. Access is limited to study staff.

viii. Controlled substances are not allowed to be stored outside Tulane University
  Department of Pharmacy.

c. **Drug Labeling for Investigational Drugs:** The following labeling requirements are
   required for Investigational New Drugs:

i. The immediate package of an investigational new Drug intended for human use
   shall bear a label with the statement “Caution: New Drug – Limited by Federal (or
   U.S.) law to investigational use.”

ii. The label or labeling of an investigational new Drug shall not bear any statement
    that is false or misleading in any particular way and shall not represent that the
    investigational new Drug is safe or effective for the purposes for which it is being
    investigated. [FDA 21 CFR 312.6].

d. **Drug Labeling for Drugs:** Louisiana rules and Tulane require that all Drugs
   dispensed shall contain a medication label with the following:

i. Patient name

ii. Identifier

iii. Protocol number or name

iv. Name of prescriber/PI

v. Strength and volume of Drug

vi. Directions for use or Administration

vii. Dose

viii. Number of units dispensed

ix. Expiration date

x. Initials of preparer

xi. Initials of pharmacist performing final check

xii. Indication that it is an Investigational Drug, if applicable

xiii. Any auxiliary stickers or warning labels

e. **Drug Administration** – Investigational Drugs shall be Administered in accordance
   with any applicable Federal or State laws and regulations and in accordance with any
   policies or procedures set forth by Tulane and TUHC. An informed consent
   document signed and dated by the subject and the PI must be in place before
   Administering the Drug.
Only a person licensed within the State of Louisiana and so authorized by their professional scope of practice shall Administer an Investigational Drug to a subject. A principal Investigator may designate the responsibility of Administering the Drug only after the designee has been given and has demonstrated an understanding of basic pharmacologic information about the Drug. This education and delegation of responsibility must be documented. Investigational Drugs are to be Administered in accordance with Research Protocol and in accordance with any other hospital or clinic policy pertaining to the Administration of Investigational Drugs.

Regulations & Guidelines: FDA 21 CFR 312.61.

f. The PI shall report all Unanticipated Problem Involving Risks to Subjects or Others to the IRB according to the procedures outlined in Section 8. And all Protocol Violations & Protocol Deviations (see Section 9). [FDA 21 CFR 312.64].

g. For Research involving Investigational New Drugs:

i. The PI is required to inform Research Pharmacy that the IRB has approved the Protocol through submission of the IRB approval letters.

ii. The PI must inform the IRB and Pharmacy when a study involving Investigational Drugs has been terminated by the Sponsor.

iii. The PI will report to the Sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the Drug [21 CFR §312 (b)] according to the procedures in the Protocol.

iv. The PI will maintain the following:

- Current *curriculum vitae* ("CV")
- Protocol
- Records of receipt and disposition of Drugs
- List of any co-Investigators with their CV
- Certification that all physicians, dentists, and/or nurses responsible in the study have appropriate valid licenses for the duration of the investigation, and
- Case Histories with particular documentation on evidence of Drug effects. Emphasis is on toxicity and possible untoward happenings. All unexpected adverse effects are reportable; even if the Investigator considers that the event is not related to the Drug. All unexpected adverse effects shall be reported immediately to Research Pharmacy and the IRB in the manner defined by the Protocol and this document.
- IRB letters of approval.
- Other documents as outlined in the Human Subject Protection Program Standard Operating Procedures.

2. Investigator-Sponsor or Investigator-initiated studies – When a PI files an IND or IDE, the PI is considered the Sponsor and as such is accountable for all of the FDA regulatory
responsibilities and reporting obligations of both the PI and the Sponsor, as described in the FDA regulations.

An individual or group of individuals or medical center is considered a Sponsor for an investigation if they hold the IND or IDE. At Tulane University these studies are typically called “investigator initiated studies” when they involve the use of an Investigational Drug or Device or use an approved Drug or Device for investigational purposes.

The Research Plan asks the PI if he/she also acts as the Sponsor of the Research and, if so, asks him/her to affirm that he/she has reviewed and will comply with the regulatory responsibility of a Sponsor.

The Sponsors’ or the Investigator as a Sponsor’s responsibilities includes the following:

- Selecting qualified Investigators
- Providing Investigators with the information they need to conduct the investigation properly
- Ensuring proper monitoring of the investigation
- Ensuring that the FDA and (for Devices) any reviewing IRB(s) or (for Drugs) all participating Investigators are promptly informed of significant new information about an investigation.

Additionally, if the IND or IDE product will be manufactured or produced at Tulane University, the PI must submit documentation that:

- The product preparation and manufacture meets the standards for current Good Manufacturing Practice (GMP), or any modification to those standards approved by the FDA in issuing the IND or IDE.
- The GMP plan has been approved by the applicable Tulane University IO.
- The GMP plan has been reviewed and accepted by Tulane University Risk Management and Compliance Office.

The HRPO, IRB, and RCO will assist Investigators holding an IND or IDE on the Sponsor regulations and periodically conduct random audits of PIs holding an IND or IDE.

7.4.2.2 IRB

The IRB will review the Research using the same criteria it would use in considering approval of any Research involving an FDA-regulated product. [FDA 21 CFR §56.111].

7.4.3 Emergency Use

7.4.3.1 Definitions

**Emergency Use**: means 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. [FDA 21 CFR 56.102(d)]. The Emergency Use provision in the FDA regulations [FDA 21 CFR 56.204(c)] is an exemption from prior review and approval by the IRB.
**Life Threatening**: for the purposes of this Section, it means both life-threatening and Severely Debilitating. It includes 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 of 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 requiring intervention at a Convened IRB meeting of the IRB infeasible.[FDA 21 CFR 56.102; see also FDA Information Sheet: Emergency Use of an Investigation Drug or Biologic].

**Severely Debilitating**: for the purposes of this Section, it means diseases or conditions that cause major irreversible morbidity. Examples include blindness, loss of limb, loss of hearing, paralysis or stroke. [FDA 21 CFR 56.102; see also FDA Information Sheet: Emergency Use of an Investigation Drug or Biologic].

### 7.4.3.2 Emergency Exemption from Prospective IRB Approval.

If all conditions described in 21 CFR §56.102(d) exist (i.e., a Life Threatening situation exists in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval), then the Emergency Use Exemption from prospective IRB approval may be utilized. [FDA 21 CFR §56.104(c)]. The FDA acknowledges that it is 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.

Informed consent is required unless the conditions for the Emergency Use Exemption are met (see Section 7.4.6.1 for details). The IRB must be notified within 5 working days when an Emergency Use Exemption is used (include a completed IRB Application (TU Form 102)). Any subsequent use of the Test Article at the Institution is subject to IRB review. This notification must not be construed as an approval for the Emergency Use by the IRB. The HRPO Director (or designee) will review the report to verify that circumstances of the Emergency Use conformed to FDA regulations.

### 7.4.3.3 Emergency Waiver of Informed Consent

An exception under FDA regulations permits the Emergency Use of an Investigational Drug, Device, or Biologic without informed consent where the PI and an independent physician who is not otherwise participating in the Clinical Investigation certify in writing all four of the following specific conditions: The subject is confronted by a life-threatening situation necessitating the use of the Test Article. [FDA 21 CFR §50.23]. Look to see if the following conditions are met:

1. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
2. Time is not sufficient to obtain consent from the subject’s Legally Authorized Representative; and

No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject’s life.

If time is not sufficient to obtain the independent physician determination before use of the Test Article, the actions of the PI must be reviewed and evaluated in writing by an independent physician within 5-6 working days. The IRB must be notified within 5 working days when an emergency waiver is used. This notification must not be construed as an approval for the
emergency waiver by the IRB. The IRB Chair (or designee) will review the report to verify that circumstances of the emergency waiver conformed to FDA regulations.

7.4.4 Expanded Access of Investigational Drugs

FDA regulations allow certain individuals not enrolled in clinical trials to obtain expanded access to Investigational Drugs, Agents, or Biologics through the following methods:

1. **Compassionate Use:** The term “compassionate use” is erroneously used to refer to the provision of Investigational Drugs outside of an ongoing clinical trial to a limited number of patients who are desperately ill and for whom no standard alternative therapies are available. The term “compassionate use” does not, however, appear in FDA or DHHS regulations. It is preferable, instead, to use the names of the specific access programs when discussing the use of investigational articles outside of formal clinical trials.

2. **Group C Treatment Investigational New Drug:** A means for the distribution of Investigational Drugs, Agents, or Biologics to oncologists for the treatment of cancer under Protocols outside controlled clinical trials. Group C Drugs, Agents, or Biologics usually have shown evidence of relative and reproducible efficacy in a specific tumor type. Although the FDA typically grants a waiver for most Drugs used in Group C Treatment IND Protocols, Tulane IRB requires prospective IRB review and approval.

3. **Open-Label Protocol:** A study designed to obtain additional safety data, typically done when the controlled trial has ended and treatment continues. The purpose of such a study is to allow subjects to continue to receive the benefits of the Investigational Drug, Agent, or Biologic until marketing approval is obtained. Prospective IRB review and approval is required.

4. **Parallel Track:** A method approved by the FDA that expands the availability of Investigational Drugs, Agents, or Biologics as quickly as possible to persons with AIDS and other HIV-related diseases. These Drugs, Agents, or Biologics are utilized in separate Protocols that “parallel” the controlled clinical trials and are essential to establish the safety and effectiveness of these new Drugs, Agents, or Biologics. Although the Secretary of DHHS may, on a Protocol-by-Protocol basis, waive the provisions of 45 CFR Part 46 where adequate protections are provided through other mechanisms, prospective IRB review and approval is required by the Tulane IRB.

5. **Treatment IND or Biologics:** A mechanism for providing eligible subjects with Investigational Drugs (as early in the Drug development process as possible) for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. The FDA defines an immediately life-threatening disease as a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. The FDA will permit an Investigational Drug to be used under a treatment IND after sufficient data have been collected to show that the Drug “may be effective” and does not have unreasonable risks. Prospective IRB review and approval is required.

   a. There are four requirements that must be met before a treatment IND can be issued:
      i. The Drug is intended to treat a serious or immediately life-threatening disease;
      ii. There is no satisfactory alternative treatment available;
iii. The Drug is already under investigation or trials have been completed; and
iv. The trial Sponsor is actively pursuing marketing approval.

b. The FDA identifies two special considerations when a patient is to be treated under a Treatment IND:

i. **Informed Consent**: Informed consent is especially important in treatment use situations because the subjects are desperately ill and particularly vulnerable. They will be receiving medications which have not been proven either safe or effective in a clinical setting. Both the setting and their desperation may work against their ability to make an informed assessment of the risk involved. Therefore, the IRB should ensure that potential subjects are fully aware of the risks involved in participation.

ii. **Charging for Treatment IND(s)**. The FDA permits charging for the Drug, Agent, or Biologic when used in a Treatment IND. Therefore, the IRB Committee should pay particular attention to Treatment IND(s) in which the subjects will be charged for the cost of the Drugs. If subjects will be charged for use of the Test Article, economically disadvantaged persons will likely be excluded from participation. Charging for participation may preclude economically disadvantaged persons as a class from receiving access to Test Articles. The IRB should balance this interest against the possibility that unless the Sponsor can charge for the Drug, it will not be available for treatment use until it receives full FDA approval.

6. **Single-Patient Use**: The use of an Investigational Drug outside of a controlled clinical trial for a patient, usually in a desperate situation, who is unresponsive to other therapies or in a situation where no approved or generally recognized treatment is available. There is usually little evidence that the proposed therapy is useful, but may be plausible on theoretical grounds or anecdotes of success. Access to Investigational Drugs for use by a single, identified patient may be gained either through the Sponsor under a treatment Protocol, or through the FDA, by first obtaining the Drug from the Sponsor and then submitting a treatment IND to the FDA requesting authorization to use the Investigational Drug for treatment use. Prospective IRB review and approval is required (see 5 above).

7. **Emergency IND**: The Emergency Use of an unapproved Investigational Drug, Agent, or Biologic requires an emergency IND. The FDA has established mechanisms and guidance for obtaining an Emergency IND for the use of Investigational Drugs, Agents, or Biologics.

Regulations & Guidelines: FDA 21 CFR 312.7(d).

7.4.5 **Emergency Waiver of IND**

FDA regulations at 21 CFR §312.34, §312.35, and §312.36 address the need for an Investigational Drug to be used in an emergency situation that does not allow time for submission of an IND. The FDA may authorize shipment of the Drug for a specific use in such a circumstance in advance of submission of an IND. Prospective IRB review is required unless the conditions for Exemption are met (FDA 21 CFR §56.104(c) and §56.102(d)). Informed consent is required unless the conditions for Exemption are met (21 CFR §50.23). All applicable
regulations must be met including those at 21 CFR Parts 50 and 56, and 21 CFR §312.34 and §312.35.

7.4.6 Waiver of Informed Consent for Planned Emergency Research

The conduct of planned Research in life-threatening emergencies where the requirement to obtain prospective informed consent has been waived is covered by 21 CFR §50.24. The Research plan must be approved in advance by the FDA or DHHS and the IRB, and publicly disclosed to the community in which the Research will be conducted. Such studies are not allowed under the regulations covering the Emergency Use of a Test Article in a life-threatening situation. [21 CFR §56.104(c)].

To date, the Institution’s IRB has not processed any Protocols involving planned emergency Research or any Protocols requesting such an exception. Investigators should be aware that such planned emergency Research involves an extensive approval process that involves, among other requirements, consultation with representatives of the communities in which the Research will be conducted and from which Participants will be drawn, public disclosure to such communities of plans for the Research and its risks and expected benefits, and establishment of an independent data monitoring committee to exercise oversight of the Research. In view of the extensive and stringent requirements for such Research, the IRB expects Investigators who wish to use the planned emergency exception to the informed consent requirement to consult with the IRB staff prior to submission of the Protocol to the IRB for review.

7.4.6.1 For Research Subject to FDA Regulations:

The IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:

1. The Research activity is subject to regulations codified by the FDA at Title 21 CFR part 50 and will be carried out under an FDA IND or an FDA IDE.
2. The application clearly identifies the Protocols that will include subjects who are unable to consent.
3. The research subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which might include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
4. Obtaining consent is not feasible because:
   a. The subjects will not be able to give their consent as a result of their medical condition.
   b. The intervention under investigation must be administered before consent from the subjects’ Legally Authorized Representatives is feasible.
   c. There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
5. Participation in the research holds out the prospect of direct benefit to the subjects because:
   a. Subjects are facing a life-threatening situation that necessitates intervention.
   b. Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence supported the potential for the intervention to provide a direct benefit to the individual subjects.
   c. 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.

6. The clinical investigation cannot practicably be carried out without the waiver.

7. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a Legally Authorized Representative for each subject within that window of time and, if feasible, to asking the Legally Authorized Representative contacted for consent within that window rather than proceeding without consent.

8. The investigator will summarize efforts made to contact Legally Authorized Representatives and make this information available to the IRB at the time of Continuing Review.

9. The IRB has reviewed and approved consent procedures and a consent document consistent with 21 CFR 50.25. These procedures and the consent document are to be used with subjects or their Legally Authorized Representatives in situations where use of such procedures and documented is feasible.

10. The IRB has reviewed and approved 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.

11. Additional protections of the rights and welfare of the subjects will be provided, including, at least:
   a. 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.
   b. 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.
   c. 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.
   d. Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation.
   e. If obtaining consent is not feasible and a Legally Authorized Representative is not reasonably available, the investigator has committed, if feasible, to 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. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of Continuing Review.

12. 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 consent document.

13. There is a procedure to inform the 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, that he or she might discontinue the subject’s participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
14. 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.

15. 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.

16. The protocol is performed under a separate IND or IDE that clearly identified such protocols as protocols that may include subjects who are unable to consent.

17. The submission of those protocols in a separate IND or IDE is required even if an IND for the same drug product or an IDE for the same device already exists.

18. If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation.

7.4.6.2 Research Not Subject to FDA Regulations:

The IRB finds, documents, and reports to DHHS that the following conditions have been met relative to the research:

1. The IRB found and documented that the research is not subject to regulations codified by the FDA at title 21 CFR part 50.

2. The research subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

3. Obtaining consent is not feasible because:
   a. The subjects are not able to give their consent as a result of their medical condition.
   b. The intervention involves in the research is administered before consent from the subjects’ Legally Authorized Representative is feasible.
   c. There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.

4. Participation in the research held out the prospect of direct benefit to the subjects because:
   a. Subjects are facing a life-threatening situation that necessitated intervention.
   b. Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence supported the potential for the intervention to provide a direct benefit to the individual subjects.
   c. The risks associated with the research 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.

5. The research could not practicably be carried out without the waiver.

6. The proposed research protocol defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a Legally Authorized Representative for each subject within that window of time and, if feasible, asking the Legally Authorized Representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to
7. The IRB has reviewed and approved consent procedures and a consent document in accord with 45 CFR 46.116 and 46.117.
   a. These procedures and the consent document are to be used with subjects or their Legally Authorized Representative in situations where use of such procedures and documented is feasible.
   b. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject’s participation in the research consistent with the paragraph of this waiver.

8. Additional protections of the rights and welfare of the subjects are provided, including, at least:
   a. Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the research is conducted and from which the subjects are drawn.
   b. Public disclosure to the communities in which the research is conducted and from which the subjects are drawn, prior to initiation of the research, of plans for the research and its risks and expected benefits.
   c. Public disclosure of sufficient information following completion of the research to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results.
   d. Establishment of an independent data monitoring committee to exercise oversight of the research.
   e. If obtaining consent is not feasible and a Legally Authorized Representative is not reasonably available, the investigator has committed, if feasible, to 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 research.
      i. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of Continuing Review.
      ii. Procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remained 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 research, the details of the research and other information contained in the consent document.
      iii. There is a procedure to inform the subject, or if the subject remained incapacitated, a Legally Authorized Representative of the subject, or if such a representative is not reasonably available, a family member, 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.
      iv. If a Legally Authorized Representative or family member is told about the research and the subject’s condition improves, the subject is also informed as soon as feasible.
      v. If a subject is entered into research with waived consent and the subject dies before a Legally Authorized Representative or family member can be contacted,
information about the research is provided to the subject’s Legally Authorized Representative or family member, if feasible.

vi. For the purposes of this waiver “family member” means any one of the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.