# Tulane University Standard Operating Procedures for its Human Research Protection Program

1. **Human Research Protection Program (“HRPP”)** ................................................................. 11
   1.1 **Policy** ........................................................................................................................... 11
   1.2 **Mission** ........................................................................................................................ 11
   1.3 **Institutional Authority** .................................................................................................. 12
   1.4 **Definitions** .................................................................................................................... 12
   1.5 **Ethical Principles** ......................................................................................................... 14
   1.6 **Regulatory Compliance** ............................................................................................... 15
   1.7 **Federal-Wide Assurance (“FWA”)** .............................................................................. 15
   1.8 **Research Covered by the HRPP** .................................................................................. 16
   1.9 **Written Policies and Procedures** ................................................................................... 16
   1.10 **HRPP Organization** .................................................................................................... 16
       1.10.1 **University President** ............................................................................................ 17
       1.10.2 **Institutional Official (“IO”)** ................................................................................ 17
       1.10.3 **Director of the HRPO** .......................................................................................... 17
       1.10.4 **Assistant Director of the HRPO** ......................................................................... 18
       1.10.5 **University Research Compliance Officer (“RCO”)** ............................................ 18
       1.10.6 **Institutional Review Board (“IRB”)** ..................................................................... 18
       1.10.7 **The Principal Investigator (“PI”)** ......................................................................... 19
       1.10.8 **Other Related Entities & Units to HRPP** ............................................................. 20
            1.10.8.1 **Office of Research Administration (“ORA”)** ................................................. 20
            1.10.8.2 **Research Pharmacy Services** ....................................................................... 20
            1.10.8.3 **Protocol-Specific Coordination** .................................................................... 21
            1.10.8.4 **Office of General Counsel** ............................................................................. 21
            1.10.8.5 **Research Compliance Operations Committee (“RCOC”)** .......................... 21
       1.10.9 **Relationship Between Components** ...................................................................... 21
   1.11 **HRPO Operations** ....................................................................................................... 22
       1.11.1 **Human Research Protection Office (“HRPO”)** ................................................... 22
       1.11.2 **IRB Senior Program Coordinator** ......................................................................... 22
       1.11.3 **IRB Program Coordinator** .................................................................................... 22
       1.11.4 **IRB Records Coordinator** ....................................................................................... 22
1.11.5 Executive Secretary 

1.11.6 Selection, Supervision and Evaluation of HRPO Supporting Staff 

1.11.6.1 Selection Process: 

1.11.6.2 Supervision: 

1.11.6.3 Evaluation: 

1.11.7 HRPO & IRB Resources 

1.12 Research Quality Assurance/Quality Improvement Activities 

1.12.1 Institutional Audits and Compliance Reviews 

1.12.2 Reporting and Disposition 

1.12.3 Internal Compliance Reviews 

1.12.4 Quality Improvement 

2 Institutional Review Board 

2.1 Policy 

2.2 IRB Authority 

2.3 Number of IRBs 

2.4 Roles and Responsibilities—Chair of the IRB 

2.5 Roles and Responsibilities—Vice Chair of the Biomedical IRB 

2.6 Chair of IRB Subcommittee 

2.6.1 Subcommittees of the IRB 

2.7 IRB Membership 

2.7.1 Definitions 

2.7.2 Composition of the IRB 

2.7.3 Nomination & Appointment of IRB Members 

2.7.3.1 Nomination of New IRB Members 

2.7.3.2 Appointment of New IRB Members 

2.7.3.3 Documentation and Information for New IRB Members 

2.7.3.4 Periodic Review of IRB Composition and Membership 

2.7.4 Alternate IRB Members: 

2.8 IRB Member Conflict of Interest 

2.9 Use of Consultants 

2.10 Duties of IRB Members 

2.11 Attendance Requirements 

2.12 Training & Education 

2.12.1 New IRB Members—Orientation 

2.12.2 New IRB Members—Initial Education 

2.12.3 IRB Members—Continuing Education 

2.12.4 HRPO Staff—Orientation & Initial Education 

2.12.5 HRPO Staff—Continuing Education 

2.13 Insurance Coverage for Research Oversight Activity 

2.14 Review of IRB Member Performance 

2.15 Reporting and Investigation of Allegations of Undue Influence 

3 IRB Review Process 

3.1 Policy 

3.2 IRBNet 

3.2.1 Background Regarding IRB Net 

3.2.2 Mandatory Electronic Submissions
3.8.4 Independent Verification That No Material Changes Have Occurred .......................... 60
3.8.5 Consent Monitoring ................................................................................................. 61
3.8.6 Investigator Conflicts of Interest ............................................................................... 61
3.8.7 Significant New Findings ......................................................................................... 61
3.8.8 Advertisements ......................................................................................................... 62
3.8.9 Payment to Research Subjects ................................................................................ 63
3.8.10 Tulane Employees .................................................................................................. 64
3.8.11 Recruitment Incentives .......................................................................................... 64
3.9 Compliance with all Applicable Laws and Regulations .............................................. 64
3.10 Possible IRB Actions ................................................................................................. 64
  3.10.1 Approval: ............................................................................................................... 65
  3.10.2 Deferred with Minor Modifications: ..................................................................... 65
    3.10.2.1 Definitions ....................................................................................................... 65
    3.10.2.2 Policy ............................................................................................................... 65
  3.10.3 Deferred with Major Modifications: ..................................................................... 66
    3.10.3.1 Definitions ....................................................................................................... 66
    3.10.3.2 Policy ............................................................................................................... 66
  3.10.3.3 Time Limit for Submitting Requested Changes for New Research Protocol Application Deferrals (minor or major modifications) ....................................................... 66
  3.10.4 Disapproved ........................................................................................................ 67
  3.10.5 Approved in Principle .......................................................................................... 67
3.11 Study Suspension, Termination and Investigator Hold ............................................... 67
  3.11.1 Suspension or Termination .................................................................................. 67
  3.11.2 Investigator Hold .................................................................................................. 68
    3.11.2.1 Procedures ...................................................................................................... 68
  3.11.3 Protection of Currently Enrolled Participants ....................................................... 68
3.12 Continuing Review .................................................................................................... 69
  3.12.1 Approval Period ................................................................................................... 69
  3.12.2 Continuing Review Process .................................................................................. 70
  3.12.3 Expedited Review of Continuing Review ............................................................. 71
  3.12.4 Lapse in Continuing Review Approval ................................................................. 72
3.13 Amendment of an Approved Protocol ....................................................................... 72
  3.13.1 Expedited Review of Protocol Amendments/Modifications ............................... 73
  3.13.2 Convened IRB Review of Protocol Modifications ................................................ 73
  3.13.3 Changes in the Informed Consent Document ....................................................... 74
3.14 Closure of Protocols ................................................................................................. 74
3.15 Notice to PI of IRB Actions ....................................................................................... 74
3.16 Appeal of IRB Decision to Disapprove ..................................................................... 75
3.17 National Cancer Institute's Central IRB ................................................................. 75
  3.17.1 Adult and Pediatric Initiatives ............................................................................... 75
  3.17.2 PIs wishing to utilize an NCI CIRB must: ............................................................ 75
  3.17.3 When a Protocol has been Approved for CIRB Oversight .................................. 76
4 Documentation and Records .......................................................................................... 77
  4.1 Policy .......................................................................................................................... 77
  4.2 Definitions .................................................................................................................. 77
  4.3 IRB Records ............................................................................................................... 77
6.7.7 Research Not Otherwise Approvable .................................................. 99
   6.7.7.1 Research Not Funded by DHHS .................................................. 99

5.1 Policy ........................................................................................................ 85
5.2 Basic Requirements .................................................................................. 85
5.3 Securing and Documenting Informed Consent ...................................... 85
5.4 Informed Consent Process ...................................................................... 86
5.5 Basic Elements of Informed Consent ..................................................... 87
5.6 Additional Elements of Informed Consent to be Applied, as Appropriate ................................................................. 88
5.7 Documentation of Informed Consent ..................................................... 89
   5.7.1 Short Form Consent Documentation .................................................. 89
   5.7.2 Informed Consent--Document Stamp Date ....................................... 90
5.8 Consent Monitoring .................................................................................. 90
5.9 Waiver of Informed Consent .................................................................. 91
5.10 Waiver of Documentation of Informed Consent ................................. 92

6 Vulnerable Subjects in Research ............................................................... 93
   6.1 Policy ....................................................................................................... 93
   6.2 Involvement of Vulnerable Populations ............................................... 93
   6.3 Definitions ............................................................................................... 94
   6.4 Responsibilities ....................................................................................... 94
   6.5 Procedures .............................................................................................. 94
   6.5.1 Initial Review of Research Proposal .................................................. 94
   6.5.2 Continuing Review and Monitoring .................................................. 95
6.6 Research Involving Pregnant Women or Fetuses .................................. 95
   6.6.1 Definitions .......................................................................................... 95
   6.6.2 Research Not Funded by DHHS ....................................................... 95
   6.6.3 Research Funded by DHHS ................................................................. 96
6.7 Research Involving Neonates ................................................................. 97
   6.7.1 Definitions .......................................................................................... 97
   6.7.2 General Requirement Regarding Research Involving Neonates .... 97
   6.7.3 Neonates of Uncertain Viability ....................................................... 98
   6.7.4 Non-Viable Neonates ....................................................................... 98
   6.7.5 Viable Neonates ............................................................................... 98
   6.7.6 Research involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material ......................................................... 99
   6.7.7 Research Not Otherwise Approvable ............................................... 99
   6.7.7.1 Research Not Funded by DHHS .................................................... 99
<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.3.2</td>
<td>Change in Principal Investigator</td>
<td>157</td>
</tr>
<tr>
<td>12.3.3</td>
<td>Student Investigators</td>
<td>157</td>
</tr>
<tr>
<td>12.3.4</td>
<td>Research Team</td>
<td>158</td>
</tr>
<tr>
<td>12.4</td>
<td>Responsibilities</td>
<td>158</td>
</tr>
<tr>
<td>12.5</td>
<td>Training / Ongoing Education of Investigators and Research Team</td>
<td>159</td>
</tr>
<tr>
<td>12.5.1</td>
<td>Orientation</td>
<td>160</td>
</tr>
<tr>
<td>12.5.2</td>
<td>Initial Education</td>
<td>160</td>
</tr>
<tr>
<td>12.5.3</td>
<td>Waiver of Initial Education</td>
<td>160</td>
</tr>
<tr>
<td>12.5.4</td>
<td>Continuing Education and Recertification</td>
<td>160</td>
</tr>
<tr>
<td>12.5.5</td>
<td>Additional Resources</td>
<td>161</td>
</tr>
<tr>
<td>12.5.6</td>
<td>Investigator Concerns</td>
<td>161</td>
</tr>
<tr>
<td>13</td>
<td>Sponsored Research</td>
<td>162</td>
</tr>
<tr>
<td>13.1</td>
<td>Policy</td>
<td>162</td>
</tr>
<tr>
<td>13.2</td>
<td>Definitions</td>
<td>162</td>
</tr>
<tr>
<td>13.3</td>
<td>ORA Review</td>
<td>162</td>
</tr>
<tr>
<td>14</td>
<td>Conflicts of Interest in Research</td>
<td>164</td>
</tr>
<tr>
<td>14.1</td>
<td>Policy</td>
<td>164</td>
</tr>
<tr>
<td>14.2</td>
<td>Definitions</td>
<td>164</td>
</tr>
<tr>
<td>14.3</td>
<td>Initial Review</td>
<td>165</td>
</tr>
<tr>
<td>14.4</td>
<td>Continuing Review</td>
<td>165</td>
</tr>
<tr>
<td>14.5</td>
<td>Updated COIs and Failure of PIs to Complete Annual COI Form</td>
<td>166</td>
</tr>
<tr>
<td>14.6</td>
<td>IRB Review of COI</td>
<td>166</td>
</tr>
<tr>
<td>15</td>
<td>Participant Outreach</td>
<td>169</td>
</tr>
<tr>
<td>15.1</td>
<td>Policy</td>
<td>169</td>
</tr>
<tr>
<td>15.2</td>
<td>Responsibility</td>
<td>169</td>
</tr>
<tr>
<td>15.3</td>
<td>Outreach Resources and Educational Materials</td>
<td>169</td>
</tr>
<tr>
<td>15.4</td>
<td>Questions, Concerns, and Complaints</td>
<td>169</td>
</tr>
<tr>
<td>15.5</td>
<td>Evaluation</td>
<td>169</td>
</tr>
<tr>
<td>16</td>
<td>Health Insurance Portability and Accountability Act (HIPAA)</td>
<td>171</td>
</tr>
<tr>
<td>16.1</td>
<td>Historical Background</td>
<td>171</td>
</tr>
<tr>
<td>16.2</td>
<td>Health Care Component</td>
<td>171</td>
</tr>
<tr>
<td>16.3</td>
<td>Policy</td>
<td>172</td>
</tr>
<tr>
<td>16.4</td>
<td>Definitions</td>
<td>172</td>
</tr>
<tr>
<td>16.5</td>
<td>Effects of HIPAA on Research</td>
<td>174</td>
</tr>
<tr>
<td>16.6</td>
<td>Privacy Board</td>
<td>174</td>
</tr>
<tr>
<td>16.7</td>
<td>Permitted Uses and Disclosures of Research PHI</td>
<td>175</td>
</tr>
<tr>
<td>16.8</td>
<td>Research under HIPAA</td>
<td>176</td>
</tr>
<tr>
<td>16.8.1</td>
<td>Waiver of Authorization for Use or Disclosure of PHI in Research</td>
<td>176</td>
</tr>
<tr>
<td>16.8.1.1</td>
<td>Background</td>
<td>176</td>
</tr>
<tr>
<td>16.8.1.2</td>
<td>Procedure for Uses &amp; Disclosures Without an Authorization</td>
<td>176</td>
</tr>
<tr>
<td>16.8.2</td>
<td>Review Preparatory to Research</td>
<td>177</td>
</tr>
<tr>
<td>16.8.3</td>
<td>Research on PHI of Decedents</td>
<td>179</td>
</tr>
<tr>
<td>16.8.4</td>
<td>Limited Data Sets with a Data Use Agreement</td>
<td>179</td>
</tr>
<tr>
<td>16.9</td>
<td>Transition Provisions</td>
<td>181</td>
</tr>
<tr>
<td>16.10</td>
<td>HIPAA and Documentation Requirements</td>
<td>181</td>
</tr>
<tr>
<td>16.11</td>
<td>Patient Rights and Research</td>
<td>181</td>
</tr>
</tbody>
</table>
17 Collaborative Research and Off-Site Research ................................................................. 182
17.1 Background .................................................................................................................. 182
17.2 Policy .......................................................................................................................... 182
17.3 Definitions ................................................................................................................... 182
17.4 Types of Collaborations ............................................................................................... 183
17.5 Research Involving Non-Tulane Performance Sites: Cooperative Research .......... 184
17.6 Research Projects Involving Multiple Sites Where Tulane is the Lead Site/Lead Investigator .................................................................................................................. 187
17.7 Research at Geographically Separate Off-Site Location with No Cooperating Institution/Facility/Organization ................................................................. 188
17.8 Research at Geographically Separate Tulane-Owned Site with Non-Tulane Employees .................................................................................................................. 188
17.9 Sites Operating under a Formal Agreement with Tulane’s IRB ................................. 189
17.10 Negotiation of Federal Assurances for Collaborating Institutions (Applicable to Federally Funded Research) ................................................................. 189
17.11 Negotiation of an IRB Authorization Agreement with Collaborating Institutions .. 190
17.12 IRB Knowledge of Local Research Context .............................................................. 191
17.13 Responsibilities of Reviewing & Relying IRB & PI ................................................... 193
17.13.1 Reviewing IRB ....................................................................................................... 193
17.13.2 Relying IRB ........................................................................................................ 193
17.13.3 PI Duties ............................................................................................................. 193
17.14 Special Topic—International Research ..................................................................... 194
17.15 Additional Requirements for Department of Defense (DoD) or Department of Navy (DoN) Collaborative Research ................................................................. 195
18 Special Topics ................................................................................................................ 196
18.1 Certificate of Confidentiality (CoC) ........................................................................... 196
18.1.1 Statutory Basis for Protection ................................................................................ 196
18.1.2 Usage .................................................................................................................... 196
18.1.3 Limitations ........................................................................................................... 197
18.1.4 Application Procedures ....................................................................................... 197
18.2 Mandatory Reporting of Abuse and Neglect ............................................................ 198
18.2.1 Definitions ........................................................................................................... 198
18.2.2 Reporting Obligation of Abuse & Neglect .......................................................... 198
18.2.3 Confirming the Existence of Abuse or Neglect .................................................... 198
18.2.4 What is the Reporting Procedure? ...................................................................... 199
18.2.5 Immunity from civil or criminal liability ............................................................ 199
18.3 Tulane Students and Employees as Subjects ............................................................. 200
18.4 Student Research ....................................................................................................... 200
18.4.1 Human Subjects Research and Course Projects ................................................. 200
18.4.2 Individual Research Projects Conducted by Students ....................................... 201
18.4.3 Independent Study, Theses and Dissertations .................................................... 201
18.5 Oral History ............................................................................................................... 201
18.6 Public Registration of Clinical Trials ........................................................................ 203
18.6.1 Who Must Register? ......................................................................................... 203
18.6.2 Which Studies Must Be Registered? ................................................................. 203
18.6.3 When Must the Information Be Submitted? ......................................................... 204
18.6.4 How To Register a Clinical Trial? ................................................................. 204
18.6.5 What Information Must Be Submitted?......................................................... 205
18.6.6 Who Receives the Submitted Information? ....................................................... 206
18.6.7 Who Can Access the Registered Information? .................................................. 206
18.6.8 Must Information Be Included About Foreign Trial Sites? ............................... 206
18.6.9 Can Intermediaries Act on Behalf of a Sponsor? ............................................ 206
18.6.10 Can Sponsors Designate Multiple Individuals to Be Data Providers? ............... 206
18.6.11 What are the NIH Requirements for ClinicalTrials.gov Registration Information in Applications and Progress Reports? ............................................................. 206
18.6.12 How do the FDA registration requirements affect NIH funded studies? .......... 206
18.6.13 Do the FDA regulations have any special requirements for IND, IDE or BLA studies? 207
18.7 Genetic Studies .................................................................................................... 208
18.8 Research Involving Coded Private Information or Biological Specimens .......... 208
18.8.1 Who Determines If Coded Private Information (or Specimens) Constitutes Human Subjects Research ......................................................... 210
18.9 Case Reports Requiring IRB Review ................................................................. 210
19 Glossary .................................................................................................................. 211
20 Common Acronyms .............................................................................................. 228
21 Tracking Sheet for Approval, Amendment & Periodic Review for HRPP Standard Operating Procedures ................................. 230
1 Human Research Protection Program ("HRPP")

1.1 Policy
The Administrators of the Tulane Educational Fund (the “University,” “Tulane,” or “Institution”), fosters a research environment that promotes the respect for the rights and welfare of individuals recruited for, or participating in, Research conducted by its employees, faculty, staff, students and any institution or individual under the auspices of the University. In the review and conduct of Research, actions by the University will be guided by the principles (i.e., respect for persons, beneficence, and justice) set forth in the Ethical Principles and Guidelines for the Protection of Human Subjects of Research (often referred to as the “Belmont Report”).

The actions of the University also will conform to all applicable Federal, State, and local laws and regulations.

In order to fulfill this policy, the University has established a Human Research Protection Program (“HRPP”) which is administered by the Human Research Protection Office (“HRPO”). The HRPP consists of this policy, a mission statement, a statement of ethical principles, supporting policies and procedures (“SOPs”), and supporting Institutional Agents and Institutional committees.

1.2 Mission
The mission of the HRPP is to:

- Safeguard and promote the health and welfare of Human Subjects Research by ensuring that their rights, safety and well-being are protected;
- Provide initial and on-going training and quality education, timely review and monitoring of Human Subjects Research projects;
- Facilitate excellence in Human Subjects Research; and
- Cultivate a culture of awareness in the research community to ensure the highest level of protections for research Participants.

The HRPP includes mechanisms to:

- Establish a formal process to monitor, evaluate and continually improve the protection of human research Participants;
- Dedicate resources sufficient to do so;
- Exercise oversight of research protection;
- Educate Institutional Review Board (“IRB”) Committee members, IRB support staff, PIs, Investigators and research staff about their ethical responsibility to protect research Participants;
- When appropriate, intervene in Research and respond directly to concerns of research Participants; and
- Educate research Participants and the community.

1 The Belmont Report can be found at http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm.
1.3 Institutional Authority

The Tulane Human Research Protection Program operates under the authority of the University policy entitled “Human Research Protection Program” (“HRPP”) adopted on September 30, 2009. As stated in that policy, the operating procedures in these SOPs “serve as the governing procedures for the conduct and review of all Human Subjects Research Conducted Under the Auspices of Tulane.”

The HRPP policy and these SOPs are made available to all University PIs, Investigators and research staff, IRB Committee Members, IRB support staff, all components identified under the University Federal Wide Assurance (“FWA”), and all Assurances relying upon the Tulane’s IRB. The HRPP is posted on the Tulane HRPO Website at http://tulane.edu/asvpr/irb.

HRPO maintains a separate list to track when approved revisions and/or review to these SOPs are made, which list shall include an issue date, effective date, last reviewed date, and last revised date.

Regulations & Guidance: AAHRPP I.1.A.

1.4 Definitions

Terms used in these SOPs that are capitalized are considered defined terms under these SOPs with the meaning attributed to them consistent with their definition in a particular Section and in the Glossary found in Section 19.

Common Rule: refers to the “Federal Policy for the Protection of Human Subjects” that provides for the primary source of regulation of Research. It has been adopted by a number of Federal agencies. Although the Common Rule is codified by each agency separately, the text is identical to Department of Health and Human Services (“DHHS”) regulations contained in 45 CFR 46 Subpart A. For the purposes of the HRPP, references to the Common Rule will cite the DHHS regulations.

Federal-Wide Assurance (“Assurance” or “FWA”): is a written commitment by an institution to protect Human Subjects participating in Research. Under Federal regulations, any institution conducting or engaged in federally supported Research involving Human Subjects must obtain an Assurance in accordance with 45 CFR §46.103. This requirement also applies to any collaborating “performance site” institutions. Under 45 CFR §46.102 (f), an institution is “Engaged in Research” (as defined below) whenever its employees or Agents either intervene or interact with living individuals for Research purposes; or obtain, release, or access, Individually Identifiable Private Information for Research purposes.

Human Research Protection Program (“HRPP”): Tulane’s HRPP is a comprehensive system to ensure the protection of Human Subjects participating in Research. The objective of this program is to assist the institution in meeting applicable ethical principles and regulatory requirements for the protection of Human Subjects in Research.

Human Subject (“Subject,” “Participant,” “Human Participant,” “Human Research Subject”): a Human Subject is defined by the Common Rule as a living individual about whom an Investigator conducting Research obtains data through Intervention or Interaction with the individual or through Individually Identifiable Private Information. [DHHS 45 CFR §46.102(f); FDA 21 CFR §50.3(g); 21 CFR §56.102(e); 21 CFR §312.3(b)]. For purposes of this definition, the following definitions are germane:
• **“Interaction”** means communication or interpersonal contact between Investigator and subject. [DHHS 45 CFR §46.102(f)];

• **“Intervention”** means both physical procedures by which data are gathered (example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for Research purposes. [DHHS 45 CFR §46.102(f)]

For Research covered by FDA regulations [21 CFR Parts 50 and 56], Human Subject means an individual who is or becomes a Participant in a Clinical Investigation, either as a recipient of the Test Article or as a control. A subject may be in normal health or may have a medical condition or disease. [21 CFR §50.3(g), 21 CFR §56.102]. In the case of a Medical Device, a Human Subject/Participant also includes any individual on whose tissue specimen an Investigational Device is used or tested. [21 CFR §812.3(p)].

**NOTE:** The FDA definition of Human Subject differs according to the applicable regulation. [See 21 CFR §812.3(p), 21 CFR §50.3(g), §312.3(b), and §56.102(e)].

**Human Subject(s) Research:** means any activity that meets the definition of Research and involves Human Subjects as defined by either the Common Rule or FDA regulations.

**Institutional Agent:** is all individuals performing Institutionally designated activities or exercising Institutionally delegated authority or responsibility under Tulane’s FWA.

**Institutional Official (“IO”):** the University Vice President for Research (“VPR”) serves as the Institution’s IO for carrying out the HRPP. The IO is responsible for ensuring that the HRPP has the resources and support necessary to comply with all Federal regulations and guidelines that govern Human Subject Research. The IO is legally authorized to represent the Institution, is the signatory official for all Assurances, and assumes the obligations of the Institution’s Assurance.

**Institutional Review Board (“IRB”):** is an independent board(s) designated by the Institution to review, to approve the initiation of, and to conduct periodic review of Research involving Human Subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the Human Subjects. The IRB may be assigned other review functions as deemed appropriate by the Institution. This independent board is composed of medical, scientific, and non-Scientific Members.

**Investigator:** is an individual under the direction of the PI who is involved in some or all aspects in the Research project, including (1) the design of the study; (2) conduct of the study; (3) analysis and interpretation of the collected data; (4) directly involved in seeking the voluntary informed consent of potential subjects; and (5) writing of resulting manuscripts. Investigators can include physicians, scientists, nurses, Research staff members, administrative staff, teachers, and students. Investigators must be included on the FDA Form 1572 and/or the IRB Application (TU Form 102) signature page. While the FDA considers an Investigator and a PI to be synonymous, this document does not. [FDA 21 CFR §50.3(d); 21 CFR §56.102(h); 21 CFR §312.3(b)].

**Protocol:** is a document (including subsequent amendments) that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. A Protocol usually also gives the background and rationale for the trial, but this could be provided in other Protocol reference documents. [Good Clinical Practice: Consolidated Guidance (ICH-E6)] (Protocol includes initial Protocol and Protocol amendments).
**Research**: is defined by the Common Rule as a “systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge.” [DHHS 45 CFR §46.102(d); FDA 21 CFR §50.3(c) & (g)].

FDA regulations define Research as meaning any experiment that involves a Test Article and one or more Human Subjects, and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act (the “FDA Act”), or need not meet the requirements for prior submission to the FDA under these sections of the FDA Act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a Research or marketing permit. The terms Research, clinical Research, clinical study, study, and Clinical Investigation are synonymous for purposes of FDA regulations. [FDA 21 CFR §50.3(c), 21 CFR §56.102(c)].

- Experiments that must meet the requirements for prior submission to the FDA under section 505(i) of the FDA Act means any use of a Drug other than the use of an approved Drug in the course of medical practice. [21 CFR §312.3(b)].

- Experiments that must meet the requirements for prior submission to the FDA under section 520(g) of the FDA Act means any activity that evaluates the safety or effectiveness of a Device. [21 CFR §812.2(a)].

- Any activity in which results are being submitted to or held for inspection by FDA as part of an application for a Research or marketing permit is considered to be FDA-regulated Research [21 CFR §50.3(c), 21 CFR §56.102(c)].

**Research Under the Auspices of the Institution (or “Under the Auspices”):** this includes Research conducted at this Institution, conducted by or under the direction of any employee or Institutional Agent of this Institution (including students) in connection with his or her Institutional responsibilities, conducted by or under the direction of any employee or Institutional Agent of this Institution using any property or facility of this Institution, or involving the use of this Institution’s non-public information to identify or contact Human Subjects. See Section 1.4 for details.

1.5 Ethical Principles

The University is committed to ensuring that all Human Subjects Research in which it is engaged is conducted in accordance with the ethical principles stated in the Belmont Report. These principles are:

1. **Respect for Persons**, which is ensured by obtaining informed consent, consideration of Privacy, Confidentiality, and additional protections for Vulnerable Populations. Individuals should be treated as autonomous agents afforded the right to make decisions themselves. Those with decreased or diminished autonomy such as Minors, Prisoners, people who are mentally disabled or challenged are entitled to additional protections.

2. **Beneficence**, which is assured by ensuring that possible benefits are maximized and possible risks are minimized to all Human Subjects. Application of this principle involves a risk-benefit analysis in which the risks to subjects must be reasonable compared to the potential for benefit either to subjects directly or to society. Risk evaluation must include the consideration of both the probability and magnitude of harm, including psychological, physical, legal, social, and economic harm.
3. **Justice**, which is the equitable selection of subjects. The possibility for benefits and the potential burdens of the research should be equitably distributed among the potential research subjects. Application of this principle requires the close scrutiny of the enrollment process to ensure that particular classes are not selected for their compromised position or convenience to the Investigator. Such classes are welfare patients, racial and ethnic minorities or persons confined to institutions.

The University, through its HRPP and in partnership with its Research community, is responsible for ensuring the ethical and equitable treatment of all Human Subjects involved in Research under the auspices of the Institution “Research Under the Auspices of the Institution”.

As required by the sponsor, Tulane applies the ICH-GCP Guidelines found in Section E6 to human subjects research conducted under the auspices of Tulane’s IRB (either within the U.S. and abroad). This includes a system with procedures to ensure that the quality of every aspect of a clinical trial is implemented. For additional details with regard to compliance with the ICH-GCP Guidelines, refer to the HRPO policy entitled “International Conference on Harmonization (ICH) Good Clinical Practices (GCP), Applicability to Human Subjects Research.”


1.6 **Regulatory Compliance**

The University is responsible for ensuring compliance with all other applicable Federal, State, and local laws and regulations and Institutional policies with regard to Human Subjects Research. This is accomplished through, among other things, the HRPP, University Research compliance policies, and other Institutional policies.

All Human Subjects Research at the University is conducted in accordance with the following policies and regulations that fall under its authority.

1. Federal regulations for the protection of Human Research Subjects (often referred to as the “Common Rule”). [DHHS 45 CFR Part 46].

2. When Research involves articles subject to regulation by the FDA, the FDA regulations for the protection of Human Subjects [21 CFR Part 50] and Institutional Review Boards. [FDA 21 CFR Part 56].

3. Policies and procedures established by the Human Research Protections Program, IRB, including those incorporated in these SOPs. The current version of this reference may be found on the HRPO – Website at [http://tulane.edu/asvpr/irb](http://tulane.edu/asvpr/irb). Compliance with all other University policies that relate to Human Subject Research also is required.

4. The provisions of the Institution’s FWA (i.e., FWA 00002055).

1.7 **Federal-Wide Assurance (“FWA”)**

The University operates under an Assurance approved by the Federal Office for Human Research Protections (“OHRP”) issued by the Secretary of the Department of Health and Human Services (“DHHS”) as Tulane **FWA 00002055**. The University has designated two IRBs

---

2 The Common Rule can be found at [http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm).

3 For details, see [http://www.accessdata.fda.gov/scripts/cdrh/cfreach/cfm](http://www.accessdata.fda.gov/scripts/cdrh/cfreach/cfm).
registered as 00000324 (Biomedical IRB) and 00000339 (Social/Behavioral IRB) to review all Human Research Protocols.

In its FWA, the University has opted to limit the application of the FWA to Research funded by DHHS or Federal agencies that have adopted the Common Rule. While the terms of the FWA are applied by the University only to Federally sponsored Research, the policies and procedures in these SOPs apply to all Research under the auspices of the Institution involving Human Subjects, regardless of funding source.

Regulations & Guidance: DHHS 45 CFR §46.103; and AAHRPP I.3.K.

1.8 Research Covered by the HRPP

The HRPP covers all Research involving Human Subjects that is under the auspices of the University, regardless of the funding source. The Research may be externally funded, funded from University sources, or conducted without direct funding.

1.9 Written Policies and Procedures

These SOPs describe the requirements that govern Research Under the Auspices of the Institution that involves Human Subjects, as well as the requirements for submitting Research Proposals for review by the University’s IRB. This is not a static document. Instead, it is an organic document that is annually reviewed and revised by the HRPO Director, in consultation with applicable Institutional entities (e.g., the IRB, the Office of General Counsel (“OGC”), the Research Compliance Officer (“RCO”), etc). The IO ultimately is responsible for reviewing and approving all recommended revisions to these SOPs.

The HRPO Director will keep the University apprised of new information that may affect the HRPP, including laws and regulations; Institutional policies and procedures; and emerging ethical and scientific issues on its Website and through campus E-mailing lists.

These SOPs will be available on the University HRPO Website and copies will be available upon request.

Regulations & Guidance: DHHS 45 CFR §46.108; and FDA 21 CFR §56.108.

1.10 HRPP Organization

The HRPP is a comprehensive system to ensure the protection of Human Subjects participating in Research. It consists of a mission statement; ethical principles; this policy; supporting SOPs; various Institutional Agents (e.g., the IO, the HRPO Director, the RCO, Biosafety Officer, Radiation Safety Officer, Privacy Officer, Security Officer, etc); various Institutional committees (e.g., the Biomedical and Social/Behavioral IRB) and other committees or subcommittees addressing Human Subjects protection (e.g., the Biosafety Committee, Radiation Safety Committee, Pharmacy and Therapeutics Committee, Radioactive Drug Research Committee, Conflict of Interest Committee, etc). The HRPP also encompasses the actions of Institutional individuals and staff (e.g., PIs, Investigators, IRB staff, HRPO staff, Research staff, and Research pharmacy staff). The objective of this system is to facilitate the Institution in its efforts to adhere to ethical principles and regulatory requirements for the protection of Human Subjects in Research.

The following officials, administrative units, and individuals have primary responsibilities for implementing the HRPP:
1.10.1  University President
The President of the University is responsible for the overall operations at the University. The President has designated the ultimate responsibility and authority of the HRPP to the IO.

1.10.2  Institutional Official (“IO”)
The ultimate responsibility of the HRPP resides with the Vice President for Research, who serves as the IO of the HRPP. The IO is responsible for ensuring the Institution’s HRPP has the resources and support necessary to comply with all Institutional policies and with applicable Federal regulations and guidelines that govern Human Subject Research. The IO is legally authorized to represent the University and is the signatory of the FWA, and assumes the obligations of the FWA.

The IO also holds ultimate responsibility for (1) oversight of the Institution’s IRBs and all Tulane Investigators; (2) for assuring the IRB members and Investigators are appropriately knowledgeable to conduct Research in accordance with ethical standards and applicable regulations; and (3) for the development and implementation of an educational plan for IRB members, staff and Investigators.

Regulations & Guidance: AAHRPP I.2.A; and I.2.C.

1.10.3  Director of the HRPO
The Director of the HRPO (“HRPO Director”) reports to the IO and is responsible for:

1. Developing, managing and evaluating policies and procedures that ensure compliance with all Federal, State, and local regulations governing Research. This includes monitoring changes in regulations and policies that relate to Human Subjects Research protection and overseeing all aspects of the HRPP.

2. Advising the IO on key matters regarding Research at the University.

3. Implementing the HRPP.

4. Submitting, implementing and maintaining an approved FWA through the IO and OHRP.

5. Managing the finances of the HRPO.

6. Providing information to the IO regarding the needs and resources required for the HRPP operation.

7. Assisting Investigators in their efforts to carry out the University’s Research mission.

8. Developing and implementing needed improvements and ensuring follow-up of actions, as appropriate, for the purpose of managing risk in the HRPP.

9. Developing a training and education program as required and as appropriate for Investigators, subcommittee members and Research staff, and ensuring that training is completed in a timely manner.

10. Serving as the primary contact and liaison at the University for communications with Federal, State and local regulatory agencies with respect to Human Subject Research conducted under the auspices of the University’s IRB (e.g., OHRP and the FDA).
1.10.4 Assistant Director of the HRPO

The Assistant Director of HRPO (“HRPO Assistant Director“) reports directly to the HRPO Director. The HRPO Assistant Director advises the HRPO Director on day-to-day operations of the HRPO. Additional duties of the HRPO Assistant Director are:

1. Assist the HRPO Director to ensure constructive communication concerning the HRPP and IRB matters among the officials of the University, Investigators, clinical care staff, and Human Subjects as a means to maintain a high level of awareness regarding the safeguarding of the rights and welfare of the subjects.
2. AssistingInvestigators in their efforts to carry out the University’s Research mission.
3. Developing and implementing needed improvements and ensuring follow-up of actions, as appropriate, for the purposes of managing risk in the HRPP.
4. Developing training requirements as required and as appropriate for Investigators, committee members and Research staff, and ensuring that training is completed on a timely basis.

1.10.5 University Research Compliance Officer (“RCO”)

The University’s Research Compliance Officer (“RCO”) acts to oversee and ensure that, among other things, Research conducted at the University is in compliance with Research regulations applicable to the use of Human Subjects. In this capacity, the RCO (or designee) is responsible for (1) developing and implementing policies and procedures to ensure compliance with Research regulations and requirements; (2) conducting training and education regarding Research compliance topics; and (3) conducting audits and monitoring Research activity. The RCO may conduct audit site visits or conduct record audits of any study submitted to the IRB to review, for example, subject consent forms, Research Records or IRB Records.

The RCO serves as an ex-officio guest of the IRB to facilitate the IRB’s arriving at an unbiased and independent determination on the validity of any compliance deviations and violations and the appropriateness of recommended corrective measure(s). The RCO meets with the HRPO Director on at least weekly basis and the IO on a biweekly basis to discuss ongoing projects of the RCO that relate to Human Subjects Research.

When the HRPO Director (or designee) deems Protocol Exceptions and Deviations submitted to the IRB to be serious or on a continuing basis as defined in Section 9 (―Protocol Exceptions or Deviations‖) below, the HRPO Director (or designee) shall report the Exception or Deviation to the RCO for review. The RCO reviews same and investigates further, as needed, and reports to the IRB recommendations for corrective measures, as appropriate.

The RCO reviews and investigates all credible complaints and Allegations of Non-Compliance (as discussed below in Section 10 entitled “Complaints and Non-Compliance”) that are submitted to the IRB or that the RCO is made aware of. The RCO shall investigate all credible complaints and allegations and make a report, as appropriate, to the IRB with recommendation for corrective measures as appropriate.

1.10.6 Institutional Review Board (“IRB”)

Tulane has two IRBs created by the IO on behalf of the Institution. Tulane’s IO retains the authority to create or dissolve IRBs. Members of Institutional IRBs are appointed by the IO. The
IRB(s) prospectively and retrospectively reviews and makes decisions concerning all non-
Exempt Research Under the Auspices of the Institution. The IRB(s) is responsible for the
protection of rights and welfare of Human Subjects involved in Research Under the Auspices of
the Institution. It discharges this duty by complying with the requirements of the Common
Rule; Federal and State regulations; the FWA; and Institutional policies. See Section 2 for a
detailed discussion of the nature, role and duties of the IRB.

Tulane also utilizes the services of the following off-site IRBs:

- **National Cancer Institute (“NCI”) Adult Central IRB (“CIRB”):** for applicable
  cooperative oncology group Protocols involving adult subjects.
- **NCI Pediatric CIRB:** for applicable cooperative oncology group Protocols involving
  Minor subjects.

CIRB Protocols are studies that have been opened by cooperative groups such as the Children’s
Oncology Group (“COG”) or the Southwest Oncology Group (“SWOG”), and can be approved
using the facilitated review system employed by the CIRB. For additional details refer to the
following Website [www.nci.cirb.org](http://www.nci.cirb.org). (See also Section 3.17 for a complete discussion of the
CIRBs).

Currently, the University’s IRB serves as the IRB-of-record for Tulane University Hospital &
Clinic (“TUHC”) with respect to Research involving Human Subjects. In the event that Tulane
does agree to serve as the IRB-of-record this must be documented in writing through an inter-
institution agreement signed by the duly authorized representatives of each institution, with an
appropriate amendment to the other institution’s FWA to add Tulane’s IRB as the IRB-of-record.
The HRPO Director shall maintain a current list of Research involving Human Subjects where
Tulane’s IRB serves as the IRB-of-record for another institution.

### 1.10.7 The Principal Investigator (“PI”)

The Principal Investigator (“PI”) bears the ultimate responsibility for the protection of Human
Subjects who participate in Research. The PI is expected to abide by the highest ethical
standards for developing a Protocol that incorporates the principles of the Belmont Report.
He/she is expected to conduct Research in accordance with the approved Research Protocol and
to oversee all aspects of the Research by providing supervision of support staff, including
oversight of the informed consent process. All subjects must provide their informed consent and
the PI must establish and maintain an open line of communication with all Research subjects
within his/her responsibility. In addition to complying with all the policies and standards of the
governing regulatory bodies, the PI must comply with Institutional and administrative
requirements for conducting Research. The PI is responsible for ensuring that all Investigators
and Research staff completes appropriate training and must obtain all required approvals prior to
initiating Research. When Investigational Drugs or Devices are used, the PI is responsible for
providing written procedures for their storage, security, dispensing and disposal.

The PI ultimately is responsible for ensuring that no subject is enrolled before IRB approval is
issued and any related sponsor agreement is fully executed.
1.10.8 Other Related Entities & Units to HRPP

1.10.8.1 Office of Research Administration (“ORA”)

The Office of Research Administration (“ORA”) is responsible for, among other things, reviewing and negotiating agreements involving sponsored Research (e.g., grants, contracts and cooperative agreements) with Federal, State and local entities, as well as private and non-profit organizations. ORA also is responsible for ongoing compliance with the terms and provisions of the award issued by the sponsor, applicable Office of Management and Budget (“OMB”) circulars, and Institutional policies with respect to sponsored activity conducted at the University.

ORA maintains all sponsored agreements (include fully executed sponsored agreements and award notification for intramural and extramural funding) and internal documents submitted by the University as part of the application process for extramural funding. For additional details, refer to ORA’s policy entitled, “Establishing Sponsored Project Accounts.”

As an additional control, as part of the negotiating process, ORA reviews sponsored agreements involving clinical trials to ensure that the informed consent document is consistent with the sponsored agreement. ORA uses a checklist to facilitate its review of draft sponsored agreements.

Upon request, ORA will forward to HRPO copies of fully executed sponsored agreements.

1.10.8.2 Research Pharmacy Services

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 these SOPs. Furthermore, if Research is conducted on hospital premises, such Research shall be conducted in accordance with applicable hospital and medical staff policies and guidelines.

The University is affiliated with and routinely conducts Human Subjects Research at Tulane University Hospital and Clinic (“TUHC”), and such Research may also require the provision of clinical care to Research subjects in an inpatient acute care (i.e., hospital) setting. To this end, TUHC serves as a primary site for hospital-based clinical Research conducted by 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 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.

Refer to Section 7 for details regarding oversight of Research Pharmacy activity (both inpatient and outpatient) for Research Under the Auspices of Tulane’s IRB.

Regulations & Guidance: AAHRPP I.2.D.

1.10.8.3 Protocol-Specific Coordination

For Research Under the Auspices of the IRB that takes place at TUHC, Protocol-specific coordination must take place. The PI must identify services to be provided by units within TUHC. Refer to Section 13.15 for details with respect to the process for issuing project specific work orders under the Master Clinical Trials Affiliation Agreement between the University and TUHC.

1.10.8.4 Office of General Counsel

Tulane’s Office of General Counsel (“OGC”) provides advice to HRPO, the IO, and Institutional Agents, PI’s, Investigators and Research staff with respect to laws, regulations and requirements applicable to Human Subjects Research. This includes interpretation and application of Federal, State and local laws where Research is conducted. A member of the OGC sits on the Biomedical IRB and Social/Behavioral IRB as the Institution’s legal advisor.

1.10.8.5 Research Compliance Operations Committee (“RCOC”)

The Research Compliance Operations Committee (“RCOC”) periodically meets to ensure a dialogue is maintained between the various compliance entities at the University. Membership consists of the following: RCO; Associate General Counsel for Research; Director and Associate Director of the Tulane National Primate Research Center; Director of ORA; HRPO Director; Director of the Institutional Animal Care and Use Committee; Director of the University Biosafety Office; Dean of the School of Public Health and Tropical Medicine; and Chair of the School of Medicine’s Department of Microbiology and Immunology.

The RCO serves as Chair. The RCOC will act in an advisory capacity to the VPR, monitoring the effectiveness of existing research compliance programs, recommending new or revised policies as changes in requirements occur, and disseminating updated compliance information to the Research community. The IO and the RCO meet on a bi-weekly basis to discuss the progress of the RCOC’s work.

1.10.9 Relationship Between Components

The IRB functions independently of, but in coordination with, other Institutional regulatory committees. The IRB, however, makes its independent determination whether to approve or Disapprove a Protocol based upon whether or not Human Subjects are adequately protected. The IRB has review jurisdiction over all Research involving Human Subjects conducted, supported, or otherwise subject to regulation by any Federal department or agency that has adopted the Human Subjects regulations.

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of the Institution. However, those officials may not approve Research involving Human Subjects that has not been approved by the IRB.

Regulations & Guidance: AAHRPP I.2.D.
1.11 HRPO Operations

In addition to the leadership structure described above, other support staff members for the HRPO include: a full-time IRB Senior Program Coordinator; IRB Program Coordinator(s); a Records Coordinator, and Executive Secretary. There are two IRB Program Coordinators, one for the Biomedical IRB and another for the Social Behavioral IRB.

1.11.1 Human Research Protection Office (“HRPO”)

The University has established the Human Research Protections Office (“HRPO”) to administer the HRPP. The HRPO is supervised by the HRPO Director. The HRPO Director has expert knowledge in regulatory issues regarding Human Subjects and serves as the Human Protections Administrator. The HRPO Director is the primary contact and liaison at the University for communications with Federal, State and local regulatory agencies with respect to Human Subjects Research (e.g., OHRP or the FDA).

The HRPO Director oversees the HRPO staff that facilitate administration of the HRPP, activities of the IO, and the operation of the IRB(s). This includes responding to faculty, student, and staff questions about Human Subjects Research as well as organizing and documenting the IRB review process. The HRPO Director works closely with the IRB Chair(s) in the development of policy and procedures and is not a voting member of the IRB. The duties and responsibilities for all HRPO staff are found in their respective job descriptions, and their performance is evaluated on an annual basis.

The IRBs shall be supported by an adequate number of HRPO staff with knowledge, skills and abilities necessary to carry out the function of the IRB. At a minimum, this shall include the IRB Senior Program Coordinator and an IRB Program Coordinator for each IRB. The HRPO staff is physically located in the HRPO. An organization chart for HRPO may be found on the website.

Regulations & Guidance: AAHRPP II.1.D.

1.11.2 IRB Senior Program Coordinator

The IRB Senior Program Coordinator is responsible for all aspects of the IRB during the review process of a Research Proposal involving Human Subjects. This responsibility includes the review and screening of documents for Research Proposals prior to review by the IRB, as well as serving as the liaison between the Investigators and the IRB. The IRB Senior Program Coordinator reviews the IRB minutes for accuracy and ensures proper documentation of discussions including discussions and actions taken by the IRB during convened meetings.

1.11.3 IRB Program Coordinator

The IRB Program Coordinator is responsible for providing administrative and clerical support to the IRB, IRB Chairs and IRB Senior Program Coordinator as well as scheduling and coordinating all IRB functions.

1.11.4 IRB Records Coordinator

The IRB Records Coordinator is responsible for IRB record retention and for maintaining complete IRB Records, as defined in Section 4.3. This includes maintaining IRB member files as well as proof of human subjects training certifications.
1.11.5 Executive Secretary
The Executive Secretary is responsible for screening of IRB documents that are submitted to the Human Research Protection Office (HRPO). This responsibility includes the review of documents for research proposals prior to being submitted for further processing. The Executive Secretary conducts the preliminary screening using an Initial and Secondary Submission Checklist (TU Forms 301; 302) to ensure that applications are complete or if additional documents are required.

1.11.6 Selection, Supervision and Evaluation of HRPO Supporting Staff

1.11.6.1 Selection Process:
All HRPO staff that support the IRB and HRPO are selected by the HRPO Director and/or IRB Chair(s).

Depending on the position to be filled, qualification to be considered in the selection of HRPO staff include prior experience in IRB administration or another position within an HRPO (e.g., study coordinator), or, at the assistant or clerical levels, a desire to learn and be an active Participant in the regulatory, ethical, and procedural aspects that support an HRPO.

1.11.6.2 Supervision:
HRPO staff are supervised by the HRPO Director.

1.11.6.3 Evaluation:
HRPO staff are evaluated on an annual basis consistent with Institutional guidelines.

1.11.7 HRPO & IRB Resources
The HRPO is equipped with sufficient office space, meeting space, storage space and equipment to perform the functions required under the HRPP. The adequacy of personnel and non-personnel resources of the HRPO is assessed on an annual basis by the HRPO Director with the assistance of the Assistant HRPO Director and is reviewed and approved by the IO.

Tulane’s IO will ensure that sufficient resources exist to support HRPO and IRB operations, including meeting and office spaces, and staff for conducting IRB business. Office equipment and supplies, including technical support, file cabinets, computers, internet access, and copy machines, will be made available to the HRPP and IRB staff.

The adequacy of personnel and resources provided to HRPO and the IRB is assessed on an annual basis by the HRPO Director during the annual budget review process, and is reviewed and approved by the IO.

1.12 Research Quality Assurance/Quality Improvement Activities
The University engages in Quality Assurance/Quality Improvement (“QA/QI”) activities to measure and improve the effectiveness, quality, safety, and compliance of Research involving Human Subjects under the purview of Tulane’s IRB. These QA/QI efforts seek to comply with Institutional policies and procedures and applicable Federal, State and local laws. QA/QI efforts will be managed and implemented by the HRPO Director.

The HRPO Director will review the results of QA/QI activities, in consultation with the IRB Chair(s) and the IO. If any issues are identified, a corrective action plan will be developed by the
The HRPO Director and approved by the IO. The HRPO Director will have the responsibility for implementing the corrective action plan, the results of which will be evaluated by the IO.

**1.12.1 Institutional Audits and Compliance Reviews**

Directed ("for cause") audits and periodic ("not for cause") compliance reviews will be conducted to assess Investigator compliance with Federal, State and local laws, the requirements of these SOPs, and Institutional policies. This will facilitate identification of areas for improvement (e.g., new or revised policies, processes, forms and/or training).

Directed audits of IRB-approved Research studies are in response to identified concerns. Periodic compliance reviews are conducted using a systematic method to review IRB-approved Research on a regular basis. The results will be reported to the IO, HRPO Director, HRPO Assistant Director, the IRB Chair(s), and, as appropriate, to the IRB(s).

Activities of auditors during directed audits and periodic compliance reviews may include:

1. Requesting progress reports from Researchers;
2. Examining Investigator-held Research Records;
3. Contacting Human Subjects involved in Research;
4. Observing sites where Research involving Human Subjects and/or the informed consent process is being conducted;
5. Examining advertisements and other recruiting materials used in a study;
6. Reviewing projects to verify from sources other than the Researcher that no unapproved changes have occurred since previous review;
7. Monitoring conflict of interest concerns to assure the consent documents include the appropriate information and disclosures;
8. Monitoring **HIPAA Authorizations Forms** (TU Form 406) and **Consent Forms** (TU Forms 402; 403; 407); and
9. Conducting other monitoring or auditing activities as deemed appropriate by the IRB, the IRB Chair or the HRPO Director.

The IO, RCO, HRPO Director, and IRB Chair(s) will review the results of Institutional audits and compliance reviews. If any deficiencies are noted in the review, a corrective action plan will be developed by the HRPO Director and approved by the IO. The HRPO Director will have the responsibility for overseeing and implementing the corrective action plan, the results of which will be evaluated by the IO.

Audits and compliance reviews will be conducted for both University and non-University sites.

**1.12.2 Reporting and Disposition**

The results are reported to the Director and the IRB Chairs. Any non-compliance will be handled according to the procedures in Section 11 of the HRPP.

If an audit or review finds that subjects in a Research project have been exposed to unexpected serious harm, the incumbent will promptly report such findings to the Director...
and the IRB Chairs for immediate action as well as to any other appropriate Institutional official.

The following are examples of Non-Compliance that should be reported on this timeline:

1. Lack of an informed consent document signed and dated by subject;
2. Use of an unapproved, unstamped, and/or outdated informed consent document;
3. Enrolling a subject who does not meet the inclusion and exclusion criteria;
4. Use of recruitment procedures that have not been approved by the IRB;
5. Continuing Research activities after IRB approval has expired;
6. Protocol Deviations taken without prior IRB review to eliminate an apparent immediate hazard to Subjects;
7. Failure to report more than one event that requires prompt reporting to the Sponsor;
8. Failure to perform required laboratory tests or procedures that could impact upon the safety of the subject;
9. Breaches in subject confidentiality or privacy that could pose an increased risk to subjects or others;
10. An Investigator deliberately decides to follow different procedures than that set forth in the Protocol for one or more subjects;
11. Accidental distribution of incorrect study medications;

1.12.3 Internal Compliance Reviews

Internal directed (“not for cause”) audits and random internal compliance reviews will be conducted on an annual basis. The results may impact current practices and may require additional educational activities, and will be reported to the IO and HRPO Director, and, as appropriate, IRB Chair(s). Such audits may consider the following:

1. Review the IRB minutes to determine that adequate documentation of the meeting discussions has occurred. This review will include assessment of the documentation surrounding the discussion for protections of Vulnerable Populations as well as any risk-benefit ratio and consent issues that are included in the criteria for approval;
2. Assess the IRB minutes to assure that Quorum was met and maintained;
3. Assess the current AE reporting process;
4. Assess privacy provisions, according to HIPAA guidelines have been adequately reviewed, discussed and documented in the IRB minutes;
5. Evaluate the Continuing Review discussions to assure they are Substantive and meaningful and that no lapse has occurred since the previous IRB review;
6. Observe IRB meetings or other related activities;
7. Review IRB files to assure retention of appropriate documentation and consistent organization of the IRB files according to current policies and procedures;
8. Review the IRB database to ensure all fields are completed accurately;
9. Review of evaluations by the IRB members;
10. Verification of IRB approvals for collaborating institutions or external performance sites; and
11. Other monitoring or auditing activities deemed appropriate by the IRB.

1.12.4 Quality Improvement

All quality assurance reports, both research-related and HRPP-related, will be reviewed by the HRPO Director and the IO in order to determine if systemic changes are required in the HRPP to prevent re-occurrence. If so, a corrective action plan will be developed, implemented and evaluated.

Regulations & Guidance: AAHRPP I.3.L.
2 Institutional Review Board

2.1 Policy

The University has established two Institutional Review Boards ("IRBs") to ensure the protection of Human Subjects in Research Under the Auspices of the Institution. They include the following:

- **Institutional Review Board #1 – Biomedical (IRB00000324) (IORG0000197):** This IRB is delegated to review Human Subject Research for the following areas: (1) clinical trials such as Drug studies; (2) Research involving medical interventions; and (3) the prevention, treatment, or understanding of basic mechanisms of disease.

- **Institutional Review Board #1 – Social/Behavioral (IRB00000339) (IORG0000204):** This IRB is delegated to review Human Subject Research for the following areas: (1) Research involving the social sciences, such as sociology, psychology, anthropology, economics, political science, and history.

For the purposes of these SOPs, all on-site IRBs will be referred to as the "University IRB," "Institutional IRB," or "IRB". Tulane’s two on-site IRBs follow the same policies and procedures.

The University also utilizes the services of two off-site IRBs (i.e., the Adult NCI CIRB and Pediatric NCI CIRB) for review of certain cancer-related Research. The authorized off-site IRBs that serve as the IRB-of-record for Tulane University have the same authority as the on-site IRBs and all determinations and findings of the off-site IRBs are equally binding on all Research Under the Auspices of the Institution. Procedures for the off-site IRB are found in Section 3.17.

Once a Protocol is assigned to an IRB panel for review and consideration, then the responsibility of that Protocol remains with the assigned panel.

All non-Exempt Human Subjects Research Under the Auspices of the Institution must be reviewed and approved by an authorized University IRB prior to the initiation (i.e., before any subject(s) can be enrolled in the study) of Research activities.

The following describes the authority, role and procedures of the University IRBs.

**Regulations & Guidance:** DHHS 45 CFR §46.103; AAHRPP I.2.B; and I.3.K.

2.2 IRB Authority

Tulane’s policy authorizes the University’s IRBs to:

1. Approve, require modifications to secure Approval, or Disapprove all Research activities overseen and conducted under the auspices of the University;

2. Suspend or Terminate approval of Research not being conducted in accordance with the IRB(s) requirements or that had been associated with unexpected serious harm to Participants; and

3. Observe, or have a third party observe, the consent process and the conduct of the Research.
Research that has been reviewed and Approved by the IRB may be subject to further review and Suspension and Disapproval by University officials consistent with University policy (see Section 3.11). However, such officials may NOT approve Research that has not been approved by the IRB. University officials may strengthen requirements and/or conditions, or add other modifications to secure University approval or approval by another University committee. Previously approved Research Proposals and/or consent forms must be re-approved by the IRB before initiating the changes or modifications. The IRB Chair(s) makes the determination whether the changes require Convened IRB re-Review or Expedited Review.

The authorized off-site IRBs (e.g. the CIRBs that serve as the IRB-of-record for Tulane’s IRB) have the same authority as the on-site IRBs and all determinations and findings of the off-site IRBs are equally binding on all Research Under the Auspices of the Institution.


2.3 Number of IRBs

There are currently two on-site IRBs (the Biomedical and the Social/Behavioral IRBs) and two off-site IRBs (the Adult NCI CIRB and Pediatric NCI CIRB). The IO, the Director of the HRPO, and the IRB Chairs will review the activity of the Tulane IRBs on at least an annual basis and make a determination as to the appropriate numbers of IRB(s) that are needed for the Institution. This determination will be based on the evaluation of the performance of the IRB as described in Section 2.14.

2.4 Roles and Responsibilities--Chair of the IRB

The IO, in consultation and approval with the HRPO Director and, as appropriate, IRB members, appoints an IRB Chair and IRB Vice Chair to serve for renewable three-year terms. Any change in appointment, including re-appointment or removal, requires written notification from the IO. The IRB Chair and IRB Vice Chair must have previously served as members of the IRB.

The IRB Chair should be a highly respected individual, employed by the University, fully capable of managing the IRB, and the matters brought before it with fairness and impartiality. The task of making the IRB a respected part of the Institutional community will fall primarily on the shoulders of the IRB Chair. The IRB must be perceived to be fair, impartial and immune to pressure by the Institution's administration, the Investigator who’s Protocols are brought before it, and other professional and nonprofessional sources.

The criteria used to select an IRB Chair include experience with, and knowledge of, applicable Federal and State laws and regulations, and Institutional policies. This individual must be willing to commit to the IRB; must have past experience as an IRB member; and must demonstrate excellent communications skills, along with an understanding of clinical Research. The IRB Chair must also be flexible and demonstrate a thorough understanding of ethical issues involved in clinical Research.

The IRB Chair convenes and chairs the meetings of the IRB and is required to attend a majority of the convened meetings of the IRB. The IRB Chair may conduct or delegate Expedited Review of Research that qualifies for such review; review the responses of Investigators to contingencies of the IRB (to secure IRB approval); and to review and approve minor changes in previously approved Research during the period covered by the original approval. The IRB Chair may delegate such authority to the authorized IRB Vice Chair as needed.
The IRB Chair is a signatory for correspondence generated by the IRB and may delegate signatory authority to the IRB Vice Chair and/or the HRPO Director.

The IRB Chair advises the IO and the HRPO Director about IRB Member performance and competence.

The performance of the IRB Chair will be reviewed on an annual basis by the HRPO Director in consultation with the IO (as completed using the IRB Chair Evaluation form (TU Form 202). If the IRB Chair is not functioning in accordance with the IRB’s mission, policies and procedures; has an undue number of absences; or is not fulfilling the responsibilities of IRB Chair, then he/she will be removed by the IO and replaced by a suitable alternative.

Regulations & Guidance: AAHRPP II.1.D.

2.5 Roles and Responsibilities--Vice Chair of the Biomedical IRB

The Vice Chair of the IRB (“IRB Vice Chair”) is an IRB member appointed by the IO to serve as IRB Chair in the absence of the IRB Chair. The IRB Vice Chair must have the same qualifications, authority, and duties as IRB Chair.

Currently, there is a designated IRB Vice Chair for the Biomedical IRB. There is no designated IRB Vice Chair of the Social/Behavioral IRB.

2.6 Chair of IRB Subcommittee

If the IRB Chair creates one or more IRB Subcommittees, the Chair shall also appoint a Chair of the IRB Subcommittee (“IRB Subcommittee Chair”).

2.6.1 Subcommittees of the IRB

The IRB Chair(s), in consultation with the HRPO Director, may designate one or more other IRB Subcommittee of the IRB to perform duties, as appropriate, to review and undertake other IRB functions, and to make recommendations to the IRB for Research that is not Expedited. The IRB Chair(s), in consultation with the HRPO Director, will appoint IRB members to serve on each IRB Subcommittee created under this Section. The number and composition of the IRB Subcommittee members shall depend on the authority delegated by the IRB Chair(s) to such IRB Subcommittee (e.g., merely making recommendations versus decision-making authority). If the IRB Subcommittee has decision-making authority, then its members and composition must comply with the requirements specified in Section 2.7 of these SOPs. Members of the IRB Subcommittee must be experienced in terms of seniority on the IRB, and must be matched as closely as possible with their field of expertise to the study assigned to the IRB Subcommittee.

If the IRB Chair(s) create one or more IRB Subcommittees, they shall also indicate whether it is a standing or ad hoc IRB Subcommittee.

2.7 IRB Membership

IRB members are selected based on appropriate diversity, including consideration of race, gender, and cultural backgrounds; varied community involvement and affiliations; knowledge and experience with Vulnerable Populations; and with multiple, diverse professions or specialties, including both Scientific Members and Non-Scientific Members. The structure and

---

4 The membership of the IRB is based upon Federal policy requirements as described in 45 CFR 46.107 and 21 CFR 56.107.
composition of the IRB must be appropriate to the nature of the Research that is reviewed. Every effort is made to have member representation that has an understanding of the areas of specialty that encompasses the types of Research performed at the University. The University has procedures (See Section 2.9) that specifically outline the requirements for Protocol review by individuals with appropriate scientific or scholarly expertise beyond or in addition to that available through the IRB members.

In addition, the IRB will include members who are knowledgeable about and experienced in working with Vulnerable Populations (e.g., Children, Prisoners, Pregnant Women, or handicapped or mentally-disabled persons) that typically participate in University Research.

The IRB must promote respect for its advice and counsel in safeguarding the rights and welfare of Human Subjects and possess the professional competence necessary to review specific Research activities. Ideally, a single member of the IRB could exhibit a profile that fulfills multiple specific requirements for IRB composition.

Regulations & Guidance: DHHS 45 CFR §46.107; FDA 21 CFR §56.107; AAHRPP II.1.A; & II.1.D.

2.7.1 Definitions

Affiliated IRB Member: is an employee or agent of Tulane University (or a member of that person’s immediate family). Affiliated members include, but are not limited to individuals who are: Full- or part-time employees; current students; members of any governing panel or board of the institution; paid or unpaid consultants; health care providers holding credentials to practice at the institution; and, volunteers working at the institution on business unrelated to the IRB.

Alternate Member: is an individual who has the experience, expertise, background, professional competence, and knowledge comparable to that of the primary IRB member(s) whom the alternate would replace.

Non-Scientific Member: is any IRB Member who has formal education and training in a discipline generally considered to be non-scientific (e.g. humanities, law, business) and/or is engaged in an occupation or role that is generally considered to be non-scientific (e.g. law enforcement, minister).

Scientific Member: is an individual who has formal education and training as a physician or other medical professional, and M.S. and/or Ph.D. level physical, biological, or social behavioral scientists.

2.7.2 Composition of the IRB

1. The IRB will have at least five members with varying backgrounds to promote complete and adequate review of Research activities commonly conducted by the Institution.

2. The IRB will be sufficiently qualified through the experience, expertise, and diversity of its members, including consideration of race, gender, cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of Human Subjects.

3. In addition to possessing the professional competence necessary to review specific Research activities, the IRB will be able to ascertain the acceptability of proposed Research in terms of Institutional policies and regulations, applicable law, and standards.
of professional conduct and practice. The IRB will therefore include persons knowledgeable in these areas.

4. If the IRB regularly reviews Research that involves a vulnerable category of subjects, consideration will be given to the inclusion of one or more individuals on the IRB, who are knowledgeable about and experienced in working with these subjects. When Protocols involve Vulnerable Populations, the review process will include one or more individuals who are knowledgeable about or experienced in working with these Participants, either as members of the IRB or as consultants (see Section 3.6.8.7 and Section 6).

5. Every nondiscriminatory effort will be made to ensure that the IRB does not consist entirely of men or entirely of women, including the Institution's consideration of qualified persons of both sexes. The IRB shall not consist entirely of members of one profession.

6. The IRB includes at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.

7. At least one member who is not otherwise affiliated with Tulane and who is not part of the immediate family of a person who is affiliated with Tulane.

8. One member may satisfy more than one membership category.

9. The HRPO Director may be a voting member of the IRB.

Regulations & Guidance: DHHS 45 CFR §46.107; FDA 21 CFR §56.107; AAHRPP II.1.A

2.7.3 Nomination & Appointment of IRB Members

The IRB Chairs, IRB Vice Chair and/or the HRPO Director identify a need for a new and/or replacement IRB member who may be either a regular or Alternate Member of the IRB.

2.7.3.1 Nomination of New IRB Members

New IRB members may be nominated as follows:

1. By an IRB member;
2. By University Department Chairs or Unit Heads;
3. By the HRPO Director;
4. By the IRB Chair(s); and/or
5. By the IO.

The IRB Chair(s) and HRPO Director will review all supporting documentation and information submitted to identify those nominees who can provide relevant technical expertise or other pertinent qualifications as needed by the IRB Committee to review the types of Research commonly presented to the IRB Committee. All nominations and supporting documents will be forwarded for final selection by the IO.

Documents supporting final appointments along with records of continuing education will become part of the permanent membership records maintained by the Institution HRPO.
2.7.3.2 Appointment of New IRB Members

The IO, in consultation with the IRB Chair(s) and HRPO Director, is responsible for selecting individuals from the pool of appointees to serve as a new IRB member (and indicate whether regular or alternate). All appointments shall be documented by the IO in writing.

Appointments are made for a three-year period of service, after which the IO must elect to extend the member’s appointment for another three-year period. Any change in appointment, including reappointment or removal by the IO, requires written notification. Members may resign by written notification to the IRB Chair of their assigned Committee.

2.7.3.3 Documentation and Information for New IRB Members

The following items are required from each member of the IRB at initial appointment and as directed and will be made available as appropriate, upon request for audit [DHHS 45 CFR §46.107]:

1. Current curriculum vitae (“CV”) initially and upon reappointment;
2. Attendance at 70% (at minimum) of the regularly scheduled IRB meetings during the course of a year (upon reappointment). The member is to contact the HRPO of any potential absence as far in advance as possible;
3. Participation in the required initial training and new IRB member orientation must occur prior to review of any Research; and
4. Documentation of current Institutional certification in compliance education in the conduct of Human Subjects Research (e.g., CITI Training).

Documents supporting final appointments along with records of continuing education will become part of the permanent membership records maintained by HRPO. The IRB membership will be reviewed at least annually. Required changes will be reported to the OHRP. Regulations & Guidance: AAHRPP II.1.E.

Regulations & Guidance: AAHRPP II.1.E.

2.7.3.4 Periodic Review of IRB Composition and Membership

On an annual basis, the IRB Chairs and the HRPO Director shall review the membership and composition of the IRB to determine if they continue to meet regulatory and Institutional requirements (using the IRB Committee Evaluation (TU Form 203)). Required changes in IRB members will be reported to the OHRP.

2.7.4 Alternate IRB Members:

The appointment and function of Alternate Members is the same as that of regular IRB members; and the alternate’s expertise and perspective are comparable to those of the regular member. The area of expertise of the alternates should match that of the regular member such that the Federal policy requirements are met if a regular member cannot attend an IRB meeting. The role of the Alternate Member is to serve as a voting member of the IRB when the regular member is unavailable to attend a convened meeting. When an Alternate Member substitutes for a primary member, the Alternate Member will receive and review the same materials prior to the IRB meeting that the regular member received or would have received.
The IRB roster identifies the regular member(s) for whom each Alternate Member may substitute. The Alternate Member will not be counted as a voting member unless the regular member is absent. The IRB minutes will document when an Alternate Member has replaced a regular member. The length of term of the alternate will be the same as the term of the voting member.

2.8 IRB Member Conflict of Interest

No IRB Member may participate in the review (initial, continuing, or modification) of any Research project in which the member has a Conflict of Interest (“COI”), except to provide information as requested. Matters involving financial COI involving IRB members are governed by the Institution’s policy contained in the Part III, D, Part D of the Faculty Handbook entitled: "Policy of Tulane University on Conflicts of Commitment and Interest for Investigators in Human Subjects Research."

IRB members may find themselves in any of the following COI when reviewing research:

1. Where the member or consultant is involved in the design, conduct, and reporting of the research;
2. Where an immediate family member of the member or consultant is involved in the design, conduct, and reporting of the research;
3. Where the member holds significant Financial Interests (See Section 14.2 for a definition) related to the Research being reviewed; and
4. Any other situation where an IRB member believes that another interest conflicts with his or her ability to deliberate objectively on a Protocol.

It is the responsibility of each IRB member to disclose any COI with a study submitted for review, and recuse him/herself from the deliberations and vote by leaving the room, which departure is noted in the minutes.

The IRB Chair, will poll IRB members at each convened meeting to determine if a COI exists regarding any Protocols to be considered during the meeting and reminds the committee that members with conflicts should recuse themselves by leaving the room during the discussion and vote of a specific Protocol. IRB members with a conflicting interest are excluded from being counted towards Quorum. All recusals by members with COI are recorded in the minutes.

If the Conflict of Interest status of an IRB member changes during the course of a study, the IRB Member is required to declare this to the IRB Chairs and/or HRPO Director of the HRPO.

Regulations & Guidance: DHHS 45 CFR §46.107(e); FDA 21 CFR §54; 21 CFR §56.107(e); AAHRPP II.1.C.

2.9 Use of Consultants

A “Consultant” is an individual with competence in a special area that the IRB has invited to assist in the review of issues which require expertise beyond or in addition to the availability on the IRB. These individuals do not count for IRB quorum purposes and cannot vote on any issue before the IRB [45 CFR §46.107(f)].

33
When necessary, the IRB Chair or the HRPO Director may solicit advice or otherwise engage individuals to assist the IRB in its review of issues or IRB Proposals, which require appropriate scientific or scholarly expertise beyond or in addition to that available on the IRB.

The need for an outside reviewer is determined in advance of the IRB meeting by the HRPO Director, HRPO Assistant Director or IRB Chair by reviewing the IRB Proposals scheduled to be reviewed at the convened meeting. The HRPO will ensure that all relevant materials are provided to the outside reviewer prior to the convened IRB meeting.

Outside reviewers or consultants can be obtained either within or outside the University community. In the event that additional scientific or scholarly expertise cannot be obtained for a Research Proposal the IRB Chair, HRPO Director or HRPO Assistant Director will defer the Proposal to the next IRB meeting in order that appropriate review may be obtained.

The HRPO Director will review the COI Policy for IRB members (see Section 2.8) with consultants. Consultants must verbally confirm to the HRPO Director that they do not have a COI prior to review. Individuals who have a COI or whose spouse or family members have a COI in the Research will not be invited to provide consultation.

The consultant’s findings will be presented to the Convened IRB for consideration either in person or in writing. If in attendance, these individuals will provide consultation but may not participate in or observe the vote.

Ad hoc or informal consultations requested by individual members (rather than for Convened IRB Review) will be requested in a manner that protects the Researcher’s confidentiality and is in compliance with the IRB COI policy (unless the question raised is generic enough to protect the identity of the particular PI and Research Proposal).

To the extent that written statements or recommendations are provided by a consultant, a copy will be kept in IRB Records. Key information provided by consultants at meetings will be documented in the minutes. Written reviews provided by the outside reviewer will be filed with the Protocol.

Regulations & Guidance: DHHS 45 CFR §46.107(f); FDA 21 CFR §56.107(f); AAHRPP II.1.B.

2.10 Duties of IRB Members

Except for emergency IRB meetings, the agenda, submission materials, Proposals, proposed informed consent forms and other appropriate documents are distributed to IRB members at least one week prior to the convened meetings at which the Research is scheduled to be discussed. For emergency IRB meetings, these written materials will be submitted as timely as possible in advance of the scheduled IRB meeting date and time.

IRB members will treat the IRB Proposals, Protocols, and supporting data confidentially. All copies of the Protocols and supporting data are returned to the IRB staff at the conclusion of review for document destruction.

2.11 Attendance Requirements

IRB members should attend all meetings for which they are scheduled. If a member is unable to attend a scheduled meeting, they should timely inform the IRB Chair, IRB Vice Chair, or an HRPO staff member at least two weeks prior to the scheduled meeting. In the case of an
emergency, members should provide notification as soon as possible. If an IRB member is unable to attend IRB meetings for a prolonged period, then such notice should be given so that the IO, the HRPO Director and the IRB Chair can determine whether an Alternate Member is needed and, if so, such Alternate Member should be temporary or permanent.

If an IRB member is to be absent for an extended period of time, such as for a sabbatical, he or she must notify the IRB at least 30 days in advance so that an appropriate replacement can be obtained. The replacement can be temporary, for the period of absence, or permanent if the member is not returning to the IRB. If the member has a designated alternate (see Section 2.7.1 and 2.7.4), the alternate can serve during the regular member’s absence, provided the IRB has been notified in advance.

2.12 Training & Education

The University is committed to providing initial and on-going training and education for the IRB Chair(s), IRB Vice-Chair(s), and IRB members, and HRPO staff related to Research ethics concerns, these SOPs, Federal and State regulatory requirements, and the University’s policies for the protection of Human Subjects involved in Research.

Regulations & Guidance: AAHRPP I.3.A; and I.4.A.

2.12.1 New IRB Members--Orientation

New IRB members, including Alternate Members, will meet with the HRPO Director or designee and the respective IRB Chair for an informal orientation session. At the session, the new member will be given an IRB Handbook (binder) that includes copies of the following:

- Tulane’s FWA;
- Tulane’s HRPP;
- Reviewer Checklist Form;
- IRB Member Handbook;
- The Belmont Report;
- Applicable Federal & State regulations including:
  - 45 CFR Part 46 – The Common Rule
  - 21 CFR Part 50 – Protection of Human Subjects
- FDA Information Sheets Guidance;\(^5\) and
- OHRP Guidance Sheets.\(^6\)

---

\(^5\) See FDA Website at: http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/ucm113709.htm

\(^6\) See OHRP Website at: http://www.hhs.gov/ohrp/policy/index.html
2.12.2 New IRB Members—Initial Education

Before serving as a primary reviewer, a new IRB member must receive and successfully complete the Web-based initial education requirement, which consists of the CITI training modules for the protection of Human Subjects involved in Research for both biomedical and social behavioral Research.

2.12.3 IRB Members—Continuing Education

To ensure that oversight of Research involving Human Subjects is ethically grounded and the decisions made by the IRB is consistent with current regulatory and policy requirements, training is continuous for IRB members throughout their service on the IRB. Educational activities include, but are not limited to:

- In-service training at IRB meetings;
- Annual training workshops and sessions;
- Distribution of appropriate publications; and
- Identification and dissemination by the HRPO Director and/or HRPO staff of new information that might affect the HRPP, including laws, regulations, policies, procedures, and emerging ethical and scientific issues to IRB members via E-mail, mail, or during IRB meetings; Tulane will provide support to send as many IRB members as possible to attend appropriate national and regional conferences on Human Participants Research protections.

2.12.4 HRPO Staff – Orientation & Initial Education

New HRPO staff will be given an orientation binder that includes copies of the following:

- Tulane’s FWA;
- Tulane’s Policies and Procedures for the Protection of Human Subjects;
- Belmont Report;
- Applicable Federal & State regulations including:
  - 45 CFR Part 46 – The Common Rule
  - 21 CFR Part 50 – Protection of Human Subjects
- FDA Information Sheets Guidance (or a link to same at the FDA’s Website); and
- OHRP Guidance Sheets (or a link to same at the FDA’s Website).

Each new HRPO staff member is expected to successfully complete the following educational requirements:

- Tulane HIPAA Privacy training; and
- The CITI training module for the protection of Human Subjects for both biomedical and social behavioral Research.
2.12.5 **HRPO Staff—Continuing Education**

Continuing training and education is provided to HRPO staff through the following:

- Discussions of regulatory and ethical issues that arise during the processing of IRB Proposals;
- CITI refresher courses (required every three years);
- Attendance of a Convened IRB meeting (at least quarterly);
- Conferences on Human Subjects Research protections (routinely); and
- Additionally, HRPO staff members are encouraged to become CIP- or CIM–certified.

2.13 **Insurance Coverage for Research Oversight Activity**

The University maintains insurance that covers IRB members, the IRB Chairs, the IO, the HRPO Director, Institutional Agents, the RCO, and HRPO staff with respect to their acts and omissions taken within their scope of their employment/service or authorized activity taken under this document. The University’s Risk Management Department should be timely notified of any potential or actual claims.

2.14 **Review of IRB Member Performance**

IRB members performance will be reviewed on an annual basis by the IRB Chair(s) and HRPO Director, which feedback from such review shall be provided to the IRB member under review (use the **IRB Member Evaluation Form** (TU Form 203)). IRB members who are not acting in accordance with the IRB(s) mission, the HRPP or IRB policies and procedures, or who have an undue number of absences will be removed.

Regulations & Guidance: AAHRPP II.1.D.

2.15 **Reporting and Investigation of Allegations of Undue Influence**

If an IRB Chair, IRB member, or IRB staff person feels that the IRB or IRB member has been unduly influenced, then he/she shall make a confidential report to the RCO and/or HRPO Director. The allegations shall be investigated by the RCO (who shall consult with the HRPO Director and IRB Chair(s) as appropriate) to consider whether undue influence exists and, if so, determine what recommended corrective action should be taken. Such findings and recommendations will be reported to the IO for a final decision.
3 IRB Review Process

3.1 Policy

All Human Subjects Research Under the Auspices of the Institution must meet the criteria for one of the following methods for review:

- Exempt review (“Exempt” or “Exempt Review”);
- Expedited review (“Expedited” or “Expedited Review”); or
- Full review by a convened IRB (“Convened IRB Review” or “Convened IRB”).

The IRB will ensure that the Research meets all required ethical and regulatory criteria for initial and Continuing Review and any modifications of approved Research. E-mail notifications are primary source of communication regarding IRB matters.

The following describe the procedures required for the review of Research by the IRB.

3.2 IRBNet

3.2.1 Background Regarding IRB Net

Tulane has adopted IRBNet for the electronic administration and management of its IRB’s. IRBNet offers electronic management of Protocols and documents; on-line submissions; web-based Protocol sharing and collaboration; automatic notifications; the furnishing of electronic signatures; event tracking; and other important electronic features to facilitate oversight of Human Subjects protections at the Institution. The University uses IRBNet to reduce manual and paper-based procedures, streamline and standardize Protocol submission, and review processes throughout the Research lifecycle.

3.2.2 Mandatory Electronic Submissions

Effective October 16, 2009, IRBNet began accepting electronic Protocol submissions, which will apply to the November 2009 submission cycle. All Protocols (including revisions and renewals) must be submitted electronically via IRBNet, and all review decision notifications will be issued electronically via IRBNet.

3.2.3 IRBNet Reference Manual & Assistance

An IRBNet Reference Manual also is available online at http://tulane.edu/asvpr/irb. Please contact HRPO with all other questions or concerns regarding IRBNet.

3.3 Human Subjects Research Determination

The responsibility for an initial determination as to whether an activity constitutes Human Subjects Research rests with the PI. The PI should make this determination based on the definitions of Human Subject and Research contained in Section 1.4. Since the University and Sponsor will hold the PI responsible if the determination is not correct, PIs are urged to request a confirmation from HRPO that an activity does not constitute Human Subjects Research. The request may be made, by E-mail or through a formal written communication. All requests must include sufficient documentation of the activity to support a determination by HRPO.

Determinations as to whether an activity constitutes Human Subjects Research will be made according to the definitions in Section 1.4 and using the Does My Research Need IRB Approval? (TU Form 703) HRPO determinations regarding activities that are either clearly or
clearly not Human Subjects Research, based on this guidance document (TU Form 703), will be made in writing and may be made by the HRPO Director, HRPO Assistant Director, IRB Chair (or their designee). Determinations regarding less clear-cut activities will be referred to the Chair, who may make the determination or refer the matter for Convened IRB Review. If a clear determination cannot be made, then, out of an abundance of caution, the activity should be deemed to constitute Human Subjects Research for further review (e.g., Exempt, Expedited or Convened IRB Review).

Documentation of all determinations made of whether activity constitutes Human Subjects Research are recorded and maintained by HRPO. Formal submissions will be responded to in writing and a copy of the submitted materials and determination letter/E-mail will be kept on file.

Regulations & Guidance: DHHS 45 CFR §46.101(a); FDA 21 CFR §56.101; AAHRPP I.3.C.

3.4 Exempt Studies

While all Research using Human Subjects must be approved by the Institution, certain categories of Research (i.e., “Exempt Research”) do not require Convened IRB Review and approval. Exempt Research is subject to Institutional review and must be determined and approved by either the IRB Chair, HRPO Director, HRPO Assistant Director (or their designee). The following Sections will describe activity that is Exempt and the procedures for conducting Exempt Review.

3.4.1 Limitations on Exemptions

Children: Exemption for Research involving survey or interview procedures or observations of public behavior does NOT apply to Research in Children, except for Research involving observations of public behavior when the Investigator does not participate in the activities being observed.

Prisoners: Exemptions do NOT apply to Research involving Prisoners. Review is required by either a Convened IRB (with a Prisoner Representative present) or by Expedited Review with review by a Prisoner Representative.

International Research: Exemptions do NOT apply to International Research. Review is required, either by a Convened IRB or, as appropriate, the IRB Chair (or designee).

3.4.2 Categories of Exempt Research

Unless an exception exists, the following categories of Research below are considered Exempt Research and not regulated by the Common Rule (see Section 1.4) or FDA regulations (see Section 3.4.3 for FDA Exemptions). Such Research is Exempt from IRB, but requires Institutional review.

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:
   a. Research on regular and special education instructional strategies, or
   b. Research on the effectiveness of, or the comparison among instructional techniques, curricula, or classroom management methods. [45 CFR §46.101(b)(1)].
2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
   a. Information obtained is recorded in such a manner that Human Subjects can be identified, directly or through identifiers linked to the subjects; and
   b. Any disclosure of the Human Subjects responses outside the Research could reasonably place the subjects at risk of criminal or civil liability, loss of insurability or be damaging to the subject’s financial standing, employability, or reputation [see 45 CFR §46.101(b)(2) or (b)(3)].

3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2), if:
   a. The human subjects are elected or appointed public officials or candidates for public office; of
   b. Federal statute(s) require(s) without exception that the confidentiality of the personality identifiable information will be maintained throughout the research and thereafter.

4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects [45 CFR §46.101(b)(4)].

   NOTE: In order to be eligible for this exemption, all of the materials have to exist at the time the research is proposed.

5. Research and demonstration projects which are conducted by or subject to the approval of federal department or agency heads, and which are designed to study, evaluate, or otherwise examine:
   a. Public benefit or service programs;
   b. Procedures for obtaining benefits or services under those programs;
   c. Possible changes in or alternatives to those programs or procedures; or
   d. Possible changes in methods or levels of payment for benefits or services under those programs.
   e. The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older American Act).
   f. The research demonstration project must be conducted pursuant to specific federal statutory authority, there must be no statutory requirements of IRB review, the research must not involve significant physical invasions or intrusions upon the privacy of subjects’, and the exemption must be invoked only with authorization or concurrence by the funding agency.
6. Taste and food quality evaluation and consumer acceptance studies,
   a. If wholesome foods without additives are consumed; or
   b. 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 Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the US. Department of Agriculture.

Regulations & Guidance: DHHS 45 CFR §46.101(b); 45 CFR §46.301(a); 45 CFR §46.401(b); FDA 21 CFR §56.104(c)-(d); OHRP Guidance at 45 CFR §46.101(b)(5): Exemptions for Research and Demonstration Projects on Public Benefit and Service Programs; OHRP Guidance on the Involvement of Prisoners in Research (May 23, 2003) Federal Register, Vol. 48, pp. 9266-9270, March 4, 1982; AAHRPP 1.3.D

3.4.3 FDA Exemptions
The following categories of Clinical Investigations are Exempt from the FDA requirements of 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)] See Section 7.4.3 for a detailed discussion of this Exemption.

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)]

3.4.4 Additional Protections
Although Exempt Research is not covered by the Federal regulations, this Research is not Exempt from the ethical guidelines of the *Belmont Report*. The individual making the determination of Exemption will determine whether to require additional protections for subjects in keeping with the guidelines of the *Belmont Report*.

3.4.5 Procedures for Exempt Review
Reviewers will use the **Exempt Reviewer Sheet** (TU Form 509) to determine and document whether the Protocol meets the Exemption criteria.

All requests for an Exemption must include a termination date (i.e., the date upon which all Research under the Protocol will cease). The Exemption is only good until the study termination date or no longer than three years from the date of Exempt determination, after which the PI must request another Exemption. During the approval period, all amendments must be submitted prior to implementation to determine that Exemption Criteria are still met. Documentation must include the specific categories justifying the Exemption.

The following materials must be electronically submitted via IRBNet:
1. A completed Exemption Application (TU Form 104); 
2. All recruitment materials (e.g., letter of invitation, flyer, recruitment script); 
3. Protocol (e.g., detailed description of Research); 
4. Consent (e.g., script to obtain subject’s verbal agreement to participate); 
5. All surveys, questionnaires, instruments, etc.; and 
6. Letter(s) or permission from each non-University site of performance.

Either the IRB Chair or designee will review requests for Exemptions and determine whether the request meets the criteria for Exempt Research. For Exempt determination purposes, the IRB Chair may delegate review to either the HRPO Director, HRPO Assistant Director, or any IRB member qualified to review this category of submission based upon their expertise of the Protocol content and knowledge of the regulations pertaining to the Research. Individuals involved in making the determination of an IRB Exempt status of a proposed Research project cannot be involved in the proposed Research. Reviewers cannot have any apparent COI.

To document the IRB reviewer’s determination of the request for Exempt Research, he/she completes the Exempt Reviewer Sheet (TU Form 508) for Exempt Review. The IRB reviewer verifies on the form whether the submission meets the definition for Research or Clinical Investigation. If the request meets the definitions of both Human Subject and Research, the reviewer indicates whether the request for Exemption was approved or denied, and if approved, the rationale for the determination and category under which it was permitted.

Once Institutional review is completed, IRB staff will send a decision letter to the PI of the results of the review.

Studies found to be Exempt are communicated to the IRB at the next regularly convened meeting after the decision of the Exemption. An Application for Closure (TU Form 602) is required when the study has ended.

OHRP has published decision trees to help in determining whether a Research Proposal fits the criteria for Exempt Review (see HRPO Website regarding Criteria for Exempt Determination (TU Form 701); Decision Trees—Humans Subjects Regulations (TU Form 707); Types of IRB Review (TU Form 706).

3.5 Expedited Review

Expedited Review (“Expedited Review”) is used by the IRB for either of both of the following:

- Some or all of the Research appearing on the list of categories of Research eligible for Expedited Review and found by the reviewer(s) to involve no more than Minimal Risk; and/or
- Minor changes in previously approved Research during the period (of one year or less) for which approval is authorized. [DHHS 45 CFR §46.110; FDA 21 CFR §56.110(b)].

Expedited Review does not mean that Institutional review is less rigorous or happens more quickly than Convened IRB Review. OHRP has published decision trees that are available online to help in determining whether a Research Proposal fits the criteria for Expedited Review.

7 The decision tree can also be found online at: www.hhs.gov/humansubjects/guidance/decisioncharts.htm.
3.5.1 Categories of Research Eligible for Expedited Review

Inclusion on this list merely means that the activity is eligible for review through the Expedited Review procedure when the specific circumstances of the proposed Research involve no more than Minimal Risk to Human Subjects. The activities listed below should not be deemed to be of Minimal Risk simply because they are included on this list.

The Expedited Review procedure may not be used for the following:

- Where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of Privacy and breach of Confidentiality are no greater than Minimal Risk.

- The availability of Expedited Review contained in Paragraphs one (1) through nine (9) of this Section below apply regardless of the age of subjects, unless specifically excepted as noted.

The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review (i.e., Expedited Review or Convened IRB Review) used by the IRB. However, it should be noted that, while Research that involves Paragraphs one (1) through seven (7) below pertains to both Initial Review and Continuing Review, Paragraphs eight (8) and nine (9) below only pertain to Continuing Reviews.

1. Clinical studies of Drugs and Medical Devices only when condition (a) or (b) is met.
   a. Research on Drugs for which an IND [21 CFR Part 312] is not required. (NOTE: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the produce is not eligible for Expedited Review.)
   b. Research on Medical Devices for which (i) an IDE [21 CFR Part 812] is not required; or (ii) the Medical Device is cleared/approved for marketing and the Medical Device is being used in accordance with its cleared/approved labeling.

2. Collections of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
   a. From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
   b. From other adults and Children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may

---

8 The decision tree can also be found online at: www.hhs.gov/humansubjects/guidance/decisioncharts.htm.
9 63 FR 60364-60367, November 9, 1998.
not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for Research purposes by noninvasive means. Examples:
   a. Hair and nail clippings in a non-disfiguring manner;
   b. Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
   c. Permanent teeth if routine patient care indicates a need for extraction;
   d. Excreta and external secretions (including sweat);
   e. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue.
   f. Placenta removed at delivery;
   g. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
   h. Supra-and sub-gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
   i. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
   j. Sputum collected after saline mist nebulization.

4. Collection of data through non-invasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where Medical Devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the Medical Device are not generally eligible for Expedited Review, including studies of cleared Medical Devices for new indications.) Examples:
   a. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject’s privacy;
   b. Weighing or testing sensory acuity;
   c. Magnetic resonance imaging;
   d. Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography;
   e. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical
treatment or diagnosis). [NOTE: Some Research in this category may be exempt from the DHHS regulations for the protection of Human Subjects. See Exempt Categories and 454 CFR §46.101(b)(4). This listing refers only to Research that is not exempt.]

6. Collection of data from voice, video, digital, or image recordings made for Research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. [NOTE: Some Research in this category may be exempt from the DHHS regulations for the protection of Human Subjects. See Exempt Categories and 45 CFR §46.101(b)(2) and (b)(3). This listing refers only to Research that is not exempt.]

8. Continuing Review of research previously approved by the convened IRB as follows:
   a. Where
      1. The Research is permanently closed to the enrollment of new subjects;
      2. All subjects have completed all Research-related interventions; and
      3. The Research remains active only for long-term follow-up of subjects; or
   b. Where no subjects have been enrolled and no additional risks have been identified; or
   c. Where the remaining Research activities are limited to data analysis.

Of note, category (8) identifies three situations in which Research that is greater than Minimal Risk and has been initially reviewed by a convened IRB may undergo subsequent Continuing Review by the Expedited Review procedures.

For a multi-center Protocol, an Expedited Review procedure may be used by the IRB at a particular site whenever the conditions of category (8)(a), (b), or (c) are satisfied for that site. However, with respect to category 8(b), while the criterion that “no subjects have been enrolled” is interpreted to mean that no subjects have ever been enrolled at a particular site, the criterion that “no additional risks have been identified” is interpreted to mean that neither the investigator nor the IRB at a particular site has identified any additional risks from any site or other relevant source.

9. Continuing Review of Research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply by the IRB has determined and documented at a convened meeting that the research involves no greater than Minimal Risk and no additional risks have been identified.

Under Category (9), an Expedited Review procedure may be used for Continuing Review of Research not conducted under an investigational new drug application or investigational device exemption where categories (2) through (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than Minimal Risk and no additional risks have been identified. The
determination that “no additional risks have been identified” does not need to be made by the convened IRB.

3.5.2 Expedited Review Procedures

Under an Expedited Review procedure, the review may be carried out by the IRB Chair or by one or more reviewers designated by the IRB Chair from among IRB members. IRB members who serve as designees to the IRB Chair for Expedited Review will be matched as closely as possible with their field of expertise to the study under review.

On an annual basis, the IRB Chairs will designate a list of IRB members eligible to conduct Expedited Review. The designees must be experienced (having served on the IRB for at least one year) voting members of the IRB. The HRPO Director and/or HRPO Assistant Director will select expedited reviewers from that list. Selected reviewers must have the qualifications, experience, and knowledge in the content of the Protocol to be reviewed, as well as be knowledgeable of the requirements to approve Research under Expedited Review. IRB members with a COI in the Research (see Section 2.8) will not be selected to serve as expedited reviewers.

When reviewing Research under an Expedited Review procedure, the IRB Chairs, or designated IRB member(s), should receive and review all documentation that would normally be submitted for Convened IRB Review including the complete Protocol. This includes review of the following: (1) the complete Protocol, (2) for continuing review, an Application for Continuing Review (TU Form 603) that summarizes Research activities since the previous annual review (including modifications and AEs); (3) notes from pre-screening conducted by the HRPO staff; and (4) the current consent documentation. If the Research is subject to the ICH-GCP Guidelines, refer to the HRPO policy entitled “International Conference on Harmonization (ICH) Good Clinical Practices (GCP), Applicability to Human Subjects Research.”

Protocols submitted for Expedited Review will be pre-screened by HRPO staff to ensure that the Continuing Review package is complete. The reviewer(s) conducting initial or Continuing Reviews will complete the appropriate Expedited Initial Submissions Reviewer Sheet (TU Form 509) or Continuing Reviewer Sheet (TU Form 504) to determine whether the Research meets the criteria allowing review using the expedited procedure, and if so, whether the Research meets the regulatory criteria for approval. If the Research does not meet the criteria for Expedited Review, then the reviewer will indicate that the Research requires Convened IRB Review and the Protocol will be placed on the agenda for the next IRB meeting.

In reviewing the Research, the reviewers will follow the Review Procedures described in Sections 3.8 & 3.9 and may exercise all of the authorities of the IRB except that the reviewers may not disapprove the Research. A Research activity may be disapproved only after review in accordance with the non-Expedited procedure set forth below.

Reviewers will indicate approval, required modifications or referral to Convened IRB on the Expedited Initial Submission Reviewer Sheet (TU Form 509) or Continuing Reviewer Sheet (TU Form 504) and return it to the HRPO. If modifications are required, the HRPO staff will inform the Investigator by E-mail via IRBNet. If the modifications are minor, the HRPO Director may determine if the Investigator has sufficiently addressed the modifications. If the modifications are major or if the reviewer(s) request it the modified Protocol will be sent back to the IRB member(s) for further review.
In the event that Expedited Review is carried out by more than one IRB member and the expedited reviewers disagree, the IRB Chair may make a final determination. Upon the discretion of the HRPO Director or IRB Chair, the Protocol will be submitted to the IRB for Convened IRB Review.

Regulations & Guidance: DHHS 45 CFR §46.100; FDA 21 CFR §46.110; Categories of Research that May Be Reviewed by the IRB through an Expedited Review Procedure—FDA & DHHS; OHRP Guidance on Written IRB Procedures; OHRP Guidance on Use of Expedited Review Procedures; OHROP Guidance on Continuing Review; FDA Information Sheets: Continuing Review after Study Approval; AAHRPP II.2.B.

3.5.3 Informing the IRB

All members of the IRB will be apprised of all Expedited Review approvals that were reviewed by the IRB Chair or designated IRB member. This notification is accomplished by means of a list in the agenda of the next scheduled meeting. Any IRB member can request to review the full Protocol by contacting the HRPO.

3.6 Convened IRB Review

Convened IRB Review (or “Convened IRB”) means review by a fully convened IRB. Except when an Expedited Review procedure is used, the IRB will conduct initial and Continuing Reviews of all Research at convened meetings at which a Quorum (see Section 3.6.7 below) of the members is present. [FDA 21 CFR §56.108(c); AAHPRR II.2.C].

3.6.1 IRB Meeting Schedule

The IRB meets on a regular basis throughout the year. The schedule for the IRB may vary due to holidays or lack of Quorum. The schedule for IRB meetings is found on the HRPO Website www.tulane.edu/asvpr/irb. Additionally, this information is posted in the HRPO for the benefit of all Investigators, Research coordinators and other Research staff when submitting Protocol materials. Special meetings may be called at anytime by the IRB Chair and/or HRPO Director.

3.6.2 Preliminary Review

All submissions by PIs to the IRB are electronically date stamped to confirm the day and time of submission.

The HRPO Staff will perform a preliminary review of all Protocol materials submitted to the IRB for determination of completeness and accuracy. Only complete submissions will be referred for further consideration (i.e., Exempt, Expedited or Convened IRB Review).

The Investigator will be informed either by E-mail or phone of missing materials and the deadline to resubmit corrections before further review can take place. The PI is responsible to provide the HRPO with an active E-mail address and current contact information.

Specific questions regarding the HRPP policies and procedures; determining whether a particular Protocol is Human Subjects Research or not; and which forms are required for a particular study, can be submitted in writing and/or via the telephone to the HRPO for further information and/or clarification. Individual appointments with the IRB Chair, HRPO Director, HRPO Assistant Director and/or HRPO staff can also be arranged and are strongly recommended for first-time submissions.
3.6.3 Primary & Secondary Reviewers

After it has been determined that the Protocol submission is complete, the IRB Chair, with the assistance of the HRPO Staff, assigns Protocols for review based on the scientific content of the Protocol, reviewer’s area of expertise, and requirements for representation of Vulnerable Populations involved in the Research. For Protocols submitted to the Tulane Biomedical IRB, a primary and secondary reviewer will be assigned for each submission that qualifies for Convened IRB Review. Scheduled reviewers are generally assigned Protocols or other items for review at each meeting. For Protocols submitted to the Tulane’s Social/Behavioral IRB, one reviewer will be assigned to each Protocol and a reviewer may be assigned several Protocols or other Research items for review.

When the IRB is presented with a Protocol which, in the opinion of the IRB Chairs, may be outside of the knowledge base or representative capacity of all of the IRB members, an outside consultant will be sought (see Section 2.9 above). Proposals for which appropriate expertise cannot be obtained for a given meeting will be deferred to another meeting when appropriate expertise can be achieved.

Primary and secondary reviewers are responsible for:

1. Having a thorough knowledge of all details of the proposed Research;
2. Performing an in-depth review of the proposed Research and supporting documents;
3. Leading the discussion of the proposed Research at the convened meeting, presenting both positive and negative aspects of the Research, and leading the IRB through the regulatory criteria for approval (see Sections 3.8 and 3.9);
4. Making suggestions for changes to the proposed Research, where applicable; and
5. Completing all applicable IRB reviewer forms.

If the primary reviewer will be absent from the meeting, the secondary reviewer may act as the primary reviewer or a new reviewer may be assigned. The primary and secondary reviewers will submit their comments to the IRB. In the event that there is only one primary reviewer (as in the social/behavioral IRB) the Chair or the Chair’s designee will serve as the primary reviewer. In addition, all IRB members have access to all information available to reviewers.

It should be noted that all IRB members have access to and are expected to review all IRB Proposals, not just the ones they are responsible for reviewing.

After the Convened IRB Meeting, primary and secondary reviewers must complete the Deferred MAJOR Reviewer Sheet (TU Form 506) or Deferred MINOR Reviewer Sheet (TU Form 507), as appropriate, if the IRB recommended deferring IRB approval.

3.6.4 IRB Agenda

The meeting agenda for the IRB(s) will be prepared by the HRPO Staff under the supervision of the HRPO Director and in consultation with the IRB Chair. The IRB agenda will be distributed to the IRB members prior to the scheduled meeting.

3.6.5 Pre-Meeting Distribution of Documents to IRB Members

IRB members must have sufficient time in advance of an IRB meeting to review documents in connection with IRB agenda items. For this reason, the HRPO staff must furnish all required
materials to IRB members at least five (5) days before the scheduled date upon which the IRB meeting will take place (except for emergency IRB meetings in which the material should be furnished with as much advance lead-time as reasonable).

All items for Convened IRB Review are available via IRBNet to IRB members prior to the meeting. The IRB agenda and minutes from the last meeting are available electronically for viewing during each meeting, but are removed at the conclusion of the IRB meeting to ensure Confidentiality.

Each IRB member will be given access to the following documentation, as applicable, for all Protocols on the agenda:

- The IRB agenda for the upcoming meeting;
- Minutes from the previous month’s meeting;
- Educational materials (as appropriate);
- Convened IRB initial submissions;
- Convened IRB Continuing Reviews;
- Any Deferred and/or compliance items for discussion; and
- Applicable business items and items related to audits.

In addition, each IRB member will be given access to the following documentation, as applicable, for each Protocol on the agenda:

- **IRB Initial Application** (TU Form 102);
- Proposed **Consent Form** (TU Form 402; 403; 407), **Assent Form(s)** (TU Form 401), and **HIPPA Authorization** (TU Form 405) as applicable;
- Recruitment materials/subject information, advertisements;
- Data collection instruments (including all surveys and questionnaires);
- **FDA Form 1572**;
- **Disaster Letter-Wallet Card** (TU Form 404); and
- For Research subject to ICH-GCP requirements, the Investigator’s *curriculum vitae*.

IRB members have electronic access to all materials provided to the primary and secondary reviewers.

If an IRB member requires additional information to complete the review they may contact the Investigator directly or may contact the HRPO to make the request of the Investigator.

Regulations & Guidance: AAHRPP II.1.F; II.2.D; ICH-GCP 8.2.10.

### 3.6.6 Pre-Meeting Distribution of Documents to Reviewers

Although IRBNet permits all members to review all materials submitted for review, at least one primary and/or one secondary reviewer must review: Any relevant grant applications; the sponsor’s Protocol (when one exists); the investigator’s brochure (when one exists); the DHHS-
approved sample informed consent document (when one exists); and the complete DHHS-approved Protocol (when one exists).

Protocol reviewers will use the Initial Submission Reviewer Sheet (TU Forms 502, 510) and, if investigator brochures are involved, a Correspondence Reviewer Sheet (TU Form 505) as a guide to completing their review.

### 3.6.7 Quorum

A quorum (“Quorum”) consists of a simple majority (more than fifty percent (50%) of the voting IRB membership, including at least one member whose primary concern is in a non-scientific area. If a regular IRB member and his/her alternative are present at a Convened IRB meeting, only one counts towards the quorum and the IRB member (not the alternate) is the only one entitled to vote.

Additional Quorum requirements include the following:

1. If Research involving an FDA-regulated article is involved, a licensed physician must be included in the Quorum. The physician must be present and a voting IRB member who is present for the discussion and for the review of any studies (including Initial Review, Continuing Review, modification, or report of anticipated problems involving risks to Participants and others) that involve the FDA-regulated article; and

2. When reviewing a Protocol in which a Prisoner is a subject or potential subject, at least one IRB member present at the meeting shall be a Prisoner, or a Prisoner advocate/representative with appropriate background and experience to serve in that capacity. The Prisoner/prisoner representative must be a voting IRB member who is present for the discussion and for the review of any studies (including Initial Review, Continuing Review, modification, or report of Unanticipated Problems Involving Risks to Participants and Others) that involve Prisoners.

3. For Research that involves mentally disabled persons or persons with impaired decision-making capacity, IRB membership must include at least one member who is an expert in the area of the Research.

At meetings of the IRB, a Quorum must be established and maintained for the deliberation and vote on all matters requiring a vote. The IRB Chair, with the assistance of the HRPO staff, will confirm that an appropriate Quorum is present before calling the meeting to order. The IRB Chair will be responsible to ensure that the IRB meeting remains appropriately convened. If a Quorum is not maintained, the Proposal or pending action item must be deferred or the meeting terminated. The HRPO staff and HRPO Director document the time of arrival and departure for all IRB members and notify the IRB Chair if a Quorum is not present. A Quorum Worksheet (TU Form 901) is completed by the IRB Staff and/or IRB Chair in advance of the IRB meeting to determine if a Quorum exists to convene an IRB meeting. A Sign-In Sheet (TU Forms 902, 903) is completed by IRB members, guests and ex-officio guests to document their attendance at a convened IRB meeting and to memorialize that a Quorum was appropriately convened and maintained.

IRB members are considered present and participating at a duly convened IRB meeting when either physically present or participating through electronic means (e.g., teleconferencing or video conferencing) that permits them to listen to and speak during IRB deliberations and voting.
When not physically present, the IRB member must have received all pertinent materials prior to the meeting and must be able to participate actively and equally in all discussions.

Opinions of absent IRB members that are transmitted by mail, voicemail, facsimile or E-mail may be considered by the attending IRB members, but may not be counted as votes or to satisfy the Quorum for convened meetings.

HRPO staff contact IRB members by E-mail and/or Outlook calendar approximately 7–10 days before a scheduled IRB meeting date to confirm their planned attendance to ensure appropriate notification of IRB Alternate Members.

3.6.8 IRB Meeting Procedures

3.6.8.1 Call to Order and Quorum

The IRB Chair (or designee in the event that the IRB Chair is absent) will call the IRB meeting to order, once it has been determined that a Quorum exists.

3.6.8.2 Conflict of Interest of IRB Members

Where there is a COI involving an IRB member, the IRB Chair (or designee) will remind the IRB member to recuse him/herself from the discussion and vote by leaving the room when there is a conflict for the particular action item under review.

3.6.8.3 Review & Approval of Prior Meeting Minutes

The IRB will review and discuss the IRB meeting minutes from the previous meeting and determine if there are any revisions/corrections to be made. If there are no changes to be made, the minutes will be accepted as presented and considered final. If it is determined that revisions/corrections are necessary, the minutes will be amended and presented for approval at the next IRB meeting. A majority of the members present at a duly constituted IRB meeting is required to accept the minutes.

3.6.8.4 Initial & Continuing Review & Requests for Modification

The IRB reviews all submissions for Initial Review and Continuing Review, as well as requests for modifications. The primary reviewer (and secondary reviewer for the Biomedical IRB) present an overview of the Research and lead the IRB through a discussion of the criteria approval for Research in the Initial Submission Reviewer Sheet (TU Forms 502, 510). All IRB members present at a duly convened IRB meeting have full voting rights, except in the case of a COI (see Section 2.8). In order for the Research to be approved, it must receive the approval of a majority of those voting members present at a duly constituted IRB meeting.

Regulations & Guidance: DHHS 45 CFR §46.103(b)(4); 45 CFR §46.108(b); 45 CFR §46.109; 45 CFR §46.116(b)(5); FDA 21 CFR §50.25(b)(5); 21 CFR §56.108; OHRP Guidance on Written IRB Procedures; OHRP Guidance on Continuing Review; FDA Information Sheets: Continuing Review After Study Approval; AAHRPP II.2.A.

3.6.8.5 Recording of Proceedings

It is the responsibility of the IRB Program Coordinators to record the proceedings of the IRB meeting. In addition, the IRB Program Coordinators are responsible for taking minutes at each IRB meeting.
In order for Research activity to be approved, it must receive the approval of a majority of those members present at a duly constituted IRB meeting. The recording of the vote by IRB members will denote the number of votes for, against, and abstained.

3.6.8.6 Consultant Advice--Children

When reviewing a Protocol involving Children, the IRB will ensure that appropriate pediatric expertise is available to review the specific Research activities. Non-voting consultants may be invited to assist with the review if additional expertise is needed.

3.6.8.7 Consultant Advice—Vulnerable Populations

When reviewing studies with other Vulnerable Populations, including Pregnant Women, Fetuses, Neonates, handicapped persons, and cognitively impaired, the IRB will request review by expert consultant, as needed. If the IRB regularly reviews Research involving a vulnerable category of subjects, one or more individuals who are knowledgeable about and experienced in working with these subjects should be included as IRB members (refer to policy on Vulnerable Subjects for more detail Section 6). For Research that involves mentally disabled persons or persons with impaired decision-making capacity, IRB membership must include at least one member who is an expert in the area of the Research.

3.6.8.8 Prisoner Representatives

When reviewing a Protocol in which a Prisoner is a subject:

- A majority of the IRB (exclusive of Prisoner members or Prisoner advocates) must have no association with the prison(s) involved, apart from their membership on the IRB.
- At least one IRB member present at the meeting shall be a Prisoner, or a Prisoner advocate/representative with appropriate background and experience to serve in that capacity. Prisoner/prisoner representative must be present and a voting member. The Prisoner/prisoner representative must be present for the discussion and for the review of any studies (including Initial Review, Continuing Review, modification, or report of anticipated problems involving risks to Participants and others) that involve Prisoners. The Prisoner/prisoner representative is a voting member.

3.6.9 Guests & Ex Officio Guests

At the discretion of the IRB, the PI (or designee such as a sub-investigator) may be invited to the IRB meeting to answer questions about their proposed or ongoing Research. The PI may not be present for the discussion or vote on the study or action under review by the IRB.

Other invited guests may be permitted to attend IRB meetings at the discretion of the IRB Chair and/or HRPO Director. Invited guests may not speak unless requested by the IRB and must sign a confidentiality agreement prior to the convened meeting.

Certain *ex officio* individuals (e.g., University Counsel, the RCO, and HRPO staff) regularly attend IRB meetings as *ex officio* guests. While they are not voting members of the IRB, they may participate in the IRB discussion and may provide additional information to the IRB. They need only sign a confidentiality agreement once.
3.7 Criteria for IRB Approval of Research

At the time of initial and continuing review, the IRB must determine that the following requirements are satisfied in order to approve Research involving Human Subjects:

- Risks to subjects are minimized:
  - By using procedures which are consistent with sound Research design and which do not unnecessarily expose subjects to risk; and
  - Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the Research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the Research). The IRB should not consider possible long-range effects of applying knowledge gained in the Research (e.g., the possible effects of the Research on public policy) as among those Research risks that fall within the purview of its responsibility.

- Selection of subjects is equitable. In making this assessment, the IRB should take into account the purpose of the Research and the setting in which the Research will be conducted and should be particularly cognizant of the special problems of Research involving Vulnerable Populations, such as Children, Prisoners, Pregnant Women, mentally-disabled persons, or economically- or educationally-disadvantaged persons.

- Informed consent will be sought from each prospective subject or the subject’s Legally Authorized Representative, in accordance with, and to the extent required by 45 CFR §46.116. Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR §46.117.

- When appropriate, the Research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects.

- When appropriate, there are adequate provisions to protect the Privacy of subjects and to maintain the Confidentiality of data.

- When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as Children, Prisoners, Pregnant Women, mentally-disabled persons, or economically- or educationally-disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

Regulations & Guidance: DHHS 45 CFR §46.111; FDA 21 CFR §56.111.

3.7.1 Risk-Benefit Assessment

The goal of a risk-benefit assessment is to ensure that the risks to Research subjects posed by participation in a Research study are justified relative to the anticipated benefits for the subjects or society. The IRB must:

- Judge whether the anticipated benefit, either of new knowledge or of improved health for the Research subjects, justifies asking any person to undertake the risks; and
• Disapprove Research in which the risks are judged unreasonable in relation to the anticipated benefits.

The assessment of the risks and benefits of the proposed Research - one of the major responsibilities of the IRB - involves a series of steps:

• **Identify the risks** associated with the Research, as distinguished from the risks of therapies the subjects would receive even if not participating in Research;

• **Determine whether the risks to subjects will be minimized** to the extent possible. This can be done, for example by using procedures which are consistent with sound Research design and which do not unnecessarily expose subjects to risk. This also can be accomplished, as appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes;

• **Identify the probable benefits** to be derived from the Research;

• **Determine whether the risks to subjects are reasonable in relation to the benefits** to subjects, if any, and assess the importance of the knowledge to be gained. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the Research – as distinguished from risks and benefits of therapies subjects would receive even if not participating in the Research. The IRB should not consider possible long-range effects of applying knowledge gained in the Research (e.g., the possible effects of the Research on public policy) as among those Research risks that fall within the purview of its responsibility;

• **Ensure that potential subjects will be provided with an accurate and fair description** of the risks or discomforts and the anticipated benefits;

• **Note:** If the Research is subject to the ICH-GCP Guidelines, refer to the HRPO policy entitled “International Conference on Harmonization (ICH) Good Clinical Practices (GCP), Applicability to Human Subjects Research.”

Based on this assessment, risk associated with the Research will be classified as either Minimal Risk or greater than Minimal Risk, which will be based on the interpretation of Minimal Risk.

To the extent that placebos are involved in Research, the **Decision Tree—Placebos** (TU Form 708) can be found on the HRPO Website to provide background regarding risk-benefit considerations unique to the placebos involved in research.

*Regulations & Guidance:  DHHS 45 CFR §46.111(a); FDA 21 CFR §56.111(a); AAHRPP I.1.B; & I.4.A*

### 3.7.1.1 Scientific Merit

In order to assess the risks and benefits of the proposed Research, the IRB must determine that:

• The Research uses procedures consistent with sound Research design;

• The Research design is sound enough to reasonably expect the Research to answer its proposed question; and

• The knowledge expected to result from this Research is sufficiently important to justify the risk.
In making this determination, the IRB may draw on its own knowledge and disciplinary expertise, or the IRB may draw on the knowledge and disciplinary expertise of others, such as reviews by a funding agency, or Department/Unit Head review.

Scientific review, as confirmed by the PI’s Department/Unit Head, is a critical first-step in ensuring the merit of a study submitted for approval. Such review must determine that:

- The study is appropriately designed for the intended purpose and has scientific merit;
- The investigators are appropriately trained and competent to perform the study;
- Adequate funding space and personnel are available to perform the project; and
- The study is appropriate for the subject population to be studied.

Scientific review is documented in IRBNet by the electronic signature of the administrative official responsible for the PI’s Department/Unit with regard to the initial Protocol applications. If the PI is a Department Head, then the signature of the Dean of the school is required. If the PI is a student and a Faculty Advisor is appointed, the faculty advisor must electronically sign the package/study through IRBNet.

Regulations & Guidance: DHHS 45 CFR §46.111(a)(1); FDA 21 CFR §56.111(a)(1); AAHRPP I.1.B.

3.7.2 Equitable Selection of Subjects

The IRB determines by viewing the IRB Proposal that the selection of subjects is equitable with respect to gender, age, class, etc. The IRB will not approve a study that does not provide adequately for the equitable selection of subjects or has not provided an appropriate scientific and ethical justification for excluding classes of persons who might benefit from the Research. In making this determination, the IRB evaluates: the purpose of the Research; the setting in which the Research occurs; scientific and ethical justification for including Vulnerable Populations such as Children, Prisoners, Pregnant Women, mentally disabled persons, or economically or educationally disadvantaged persons; the scientific and ethical justification for excluding classes of persons who might benefit from the Research; and the inclusion/exclusion criteria.

At the time of the Continuing Review, the IRB will determine that the PI has followed the subject selection criteria that he/she originally set forth at the time of initial IRB review and approval.

Regulations & Guidance: DHHS 45 CFR §46.111(a)(3); FDA 21 CFR §56.111(a)(3); AAHRPP II.5.A.

3.7.2.1 Recruitment of Subjects

The PI will provide the IRB with all recruiting materials to be used in identifying Participants including recruitment methods, advertisements, and payment arrangements. See Section 3.8.8 for a discussion of IRB review of advertisements, and Section 3.8.9 for a discussion of IRB review of payments/compensation to subjects.

Regulations & Guidance: DHHS 45 CFR §46.111(a)(3); 45 CFR §46.116; FDA 21 CFR §50.20; 21 CFR §56.111(a)(3); AAHRPP II.5.B.
3.7.3  Informed Consent

The IRB will ensure that informed consent ("Consent" or "Informed Consent") will be sought from each prospective subject or the subject’s Legally Authorized Representative, in accordance with, and to the extent required by 45 CFR §46.116 and 21 CFR §50.20. See Section 5. In addition, the IRB will ensure that Consent will be appropriately documented in accordance with, and to the extent required by 45 CFR §46.117 and 21 CFR §50.27 (see Section 9 below).

Regulations & Guidance: DHHS 45 CFR §46.111(a)(4) & (a)(5); FDA 21 CFR §56.111(a)(4) & (a)(5).

3.7.4  Safety Monitoring

For all Research that is more than Minimal Risk, the Investigator must submit a safety monitoring plan. The initial plan submitted to the IRB should describe the procedures for safety monitoring, reporting of Unanticipated Problems Involving Risks to Subjects or Others, descriptions of interim safety reviews and the procedures planned for transmitting the results to the IRB. This description should include information regarding an independent Data and Safety Monitoring Board ("DSMB"), if one exists, or an explanation why an independent data safety monitor is not necessary.

The IRB determines that the data safety monitoring plan makes adequate provision for monitoring the reactions of subjects and the collection of data to ensure the safety of subjects. The overall elements of the monitoring plan may vary depending on the potential risks, complexity, size and risk involved. The method and degree of monitoring needed is related to the degree of risk involved. Monitoring may be conducted in various ways or by various individuals or groups, depending on the size and scope of the research effort. These exist on a continuum from monitoring by the PI in a small, low risk study to the establishment of an independent DSMB for a large phase III clinical trial.

The factors the IRB will consider in determining whether the safety monitoring plan is adequate for the Research are as follows:

1. Monitoring is commensurate with the nature, complexity, size and risk involved.
2. Monitoring is timely. Frequency should commensurate with risk. Conclusions are reported to the IRB.
3. For low risk studies, continuous, close monitoring by the study investigator or an independent individual may be an adequate and appropriate format for monitoring, with prompt reporting of problems to the IRB, sponsor and regulatory bodies as appropriate.
4. For an individual Safety Monitor, the plan must include:
   - Parameters to be assessed
   - Mechanism to assess the critical efficacy endpoints at intervals in order to determine when to continue, modify, or stop a study.
   - Frequency of monitoring
   - Procedures for reporting to the IRB
5. For a DSMB, the plan must include:
• The name of the Data Safety Monitoring Board
• Where appropriate, is independent from the sponsor
• Availability of written reports
• Composition of the monitoring group (if a group is to be used): experts in all scientific disciplines needed to interpret the data and ensure patient safety. Clinical trial experts, biostatisticians, bioethicists, and clinicians knowledgeable about the disease and treatment under study should be part of the monitoring group or be available if warranted.
• Frequency and content of meeting reports
• The frequency and character of monitoring meetings (e.g., open or closed, public or private).

In general, it is desirable for a DSMB to be established by the study Sponsor for Research that is blinded, involves multiple sites, involves Vulnerable Subjects, or employs high-risk interventions. For some studies the National Institutes of Health (“NIH”) require a DSMB. The IRB has the authority to require a DSMB as a condition for approval of Research where it determines that such monitoring is needed. When DSMBs are utilized, IRBs conducting continuing review of Research may rely on a current statement from the DSMB indicating that it has and will continue to review study-wide AEs, interim findings, and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB.

Regulations & Guidance: DHHS 45 CFR §46.111(a)(6); FDA 21 CFR §56.111(a)(6); AAHRPP II.4.B.

3.7.5 Privacy and Confidentiality

Under the Research regulations, the IRB is required to determine whether adequate procedures are in place to protect the Privacy of subjects and to maintain the Confidentiality of the data. This duty is unrelated to HIPAA Privacy requirements, which is addressed in Section 16.

3.7.5.1 Definitions

Confidentiality: methods used to ensure that information obtained by Researchers about their Research subjects is not improperly divulged. Do not confuse this Research term with HIPAA Privacy requirements.

Identifiable Information: for research privacy purposes, this means information where the identity of the subject is or may readily be ascertained by the Investigator or associated with the information. This term should not be confused with IIHI used with HIPAA. See Section 3.7.5.1 for details.

Individually Identifiable Private Information: is information where, for Research purposes, the identity of the subject is or may readily be ascertained by the Investigator or associated with the information.

Obtain (or “Obtaining”): means to receive or access Individually Identifiable Private Information (or identifiable specimens) for Research purposes. This includes an Investigator’s
use, study, or analysis for Research purposes of Individually Identifiable Private Information (or identifiable specimens) already in the possession of the Investigator.

**Private Information:** for research privacy purposes, this means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., a medical record). [45 CFR §46.102(f)]. Do not confuse this Research term with HIPAA Privacy requirements.

### 3.7.5.2 Privacy

The IRB must determine whether the activities in the Research constitute an invasion of Privacy. In order to make that determination, the IRB must obtain information regarding how the Investigators are getting access to subjects or subjects’ private, identifiable information (“Individually Identifiable Private Information”) and the subjects’ expectations of Privacy in the situation. Investigators must have an appropriate authorization to access subjects or the subjects’ information.

In developing strategies for the protection of subjects’ Privacy, consideration should be given to:

1. Methods used to identify and contact potential Participants;
2. Settings in which an individual will be interacting with an Investigator;
3. Appropriateness of all personnel present for Research activities;
4. Methods used to obtain information about Participants and the nature of the requested information;
5. Information that is obtained about individuals other than the “target Participants,” and whether such individuals meet the regulatory definition of Human Subject (e.g., a subject provides information about a family member for a survey); and
6. How to access the minimum amount of information necessary to complete the study.

### 3.7.5.3 Confidentiality

Confidentiality and anonymity are not the same. If anyone, including the Investigator, can readily ascertain the identity of the subjects from the data, then the Research is not anonymous and the IRB must determine if appropriate protections are in place to minimize the likelihood that the information will be inappropriately divulged. The level of Confidentiality protections should be commensurate with the potential of harm from inappropriate Disclosure.

At the time of Initial Review, the IRB ensures that the Privacy and Confidentiality of Research subjects are protected. The IRB assesses whether there are adequate provisions to protect subject Privacy and maintain Confidentiality. The IRB does this through the evaluation of the methods used to obtain information:

1. About subjects;
2. About individuals who may be recruited to participate in studies;
3. The use of personally identifiable records; and
4. The methods to protect the Confidentiality of Research data.
The PI will provide information regarding the Privacy and Confidentiality of Research subjects at the time of Initial Review through the completion of the IRB Proposal, HIPAA Authorization Form (TU Form 405), and/or other submitted, applicable materials. The IRB will review all information received from the PI and determine whether or not the Privacy and Confidentiality of Research subjects is sufficiently protected. In some cases, the IRB may also require that a Certificate of Confidentiality be obtained to additionally protect Research data from compulsory disclosure (See Section 18.1).

In reviewing Confidentiality protections, the IRB shall consider the nature, probability, and magnitude of harm that would be likely to result from a Disclosure of collected information outside the Research. It shall evaluate the effectiveness of proposed De-Identification techniques, coding systems, encryption methods, storage facilities, access limitations, and other relevant factors in determining the adequacy of Confidentiality protections.

Regulations & Guidance: DHHS 45 CFR §46.111(a)(7); FDA 21 CFR §56.111(a)(7); AAHRPP II.6.A; & II.6.B.

### 3.7.6 Vulnerable Populations

At the time of Initial Review, the IRB will consider the scientific and ethical reasons for including Vulnerable Subjects in Research. The IRB may determine and require that, when appropriate, additional safeguards are put into place for Vulnerable Subjects, such as those without decision-making capacity.

For an extensive discussion about the IRB’s review and approval process for individual populations of Vulnerable Subjects, please refer to Section 6.

Regulations & Guidance: DHHS 45 CFR §46.111(b); 45 CFR 46 Subpart B, Subpart C & Subpart D; 45 CFR §46.205; FDA 21 CFR §50.3; 21 CFR §56.111(b)-(c); 21 CFR Subpart D; AAHRPP II.4.C.

### 3.8 Additional Considerations during IRB Review and Approval of Research

#### 3.8.1 Determination of Risk

At the time of Initial Review and Continuing Review, the IRB will make a determination regarding the risks associated with the Research Proposals. Risks associated with the Research will be classified as either “Minimal Risk” or “greater than Minimum Risk” based on the absolute interpretation of Minimal Risk. The meeting minutes will reflect the IRB’s determination regarding risk levels.

Regulations & Guidance: DHHS 45 CFR §46.109(e); FDA 21 CFR §56.109(f).
3.8.3 Review More Often Than Annually

Unless specifically waived by the IRB, Research that meets any of the following criteria will require review more often than annually:

1. Significant risk, as determined by the IRB, to Research subjects (e.g., death, permanent or long lasting disability or morbidity, severe toxicity) without the possibility of direct benefit to the subjects;

2. The involvement of especially Vulnerable Populations likely to be subject to coercion (e.g., terminally ill); or

3. A history of serious or Continuing Non-Compliance on the part of the PI.

The following factors also will be considered when determining which studies require review more frequently than on an annual basis:

1. The probability and magnitude of anticipated risks to subjects;

2. The likely medical condition of the proposed subjects;

3. The overall qualifications of the PI and other members of the Research team;

4. The specific experience of the PI and other members of the Research team in conducting similar Research;

5. The nature and frequency of AEs observed in similar Research at this and other Institutions;

6. The novelty of the Research making Unanticipated AEs more likely; or

7. Any other factors that the IRB deems relevant.

In specifying an IRB approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of subjects either studied or enrolled. If a maximum number of subjects studied or enrolled is used to define the approval period, it is understood that the approval period in no case can exceed 1 year and that the number of subjects studied or enrolled determines the approval period only when that number of subjects is studied or enrolled in less than 1 year.

If an approval period of less than one year is specified by the IRB the reason for more frequent review must be documented in the minutes.

3.8.4 Independent Verification That No Material Changes Have Occurred

The IRB recognizes that protecting the rights and welfare of subjects sometimes requires that the IRB independently verify utilizing sources other than the Investigator that no material changes occurred during the IRB-designated approval period. Independent verification from sources other than the Investigator may be necessary at times (e.g., in cooperative studies, or other multi-center Research).

The IRB will determine the need for verification from outside sources on a case-by-case basis and according to the following criteria:

1. Protocols where concern about possible material changes occurred without IRB approval have been raised based on information provided in Continuing Review reports or from other sources;
2. Protocols conducted by PIs who have previously failed to comply with Federal regulations and/or the requirements or determinations of the IRB;

3. Protocols randomly selected or for “cause audit” for internal audit; or

4. Whenever else the IRB deems verification from outside sources is relevant.

The following factors also will be considered when determining which studies require independent verification:

1. The probability and magnitude of anticipated risks to subjects;

2. The likely medical condition of the proposed subjects; or

3. The probable nature and frequency of changes that may ordinarily be expected in the type of Research proposed.

In making determinations about independent verification, the IRB may prospectively require that such verification take place at predetermined intervals during the approval period, or may retrospectively require such verification at the time of Continuing Review, review of amendments and/or Unanticipated Problems.

If any material changes have occurred without IRB review and approval, the IRB will decide the corrective action to be taken.

3.8.5 Consent Monitoring

In reviewing the adequacy of subject informed consent procedures for proposed Research, the IRB may on occasion determine that special monitoring of the consent process by an impartial observer (i.e., a consent monitor) is required to reduce the possibility of coercion and undue influence.

Such monitoring may be particularly warranted when the Research presents significant risks to subjects, or if subjects are likely to have difficulty understanding the information that will be provided. Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with a particular Investigator or a Research project.

See Section 5.8 for a detailed discussion of consent process monitoring.

Regulations & Guidance: DHHS 45 CFR §46.109(e); FDA 21 CFR §56.109(f); AAHRPP II.7.G.

3.8.6 Investigator Conflicts of Interest

The Research application asks Protocol-specific questions regarding COIs for Investigators and key Research personnel. As part of its review process, the IRB notifies the University’s Office of Conflict of Interest ("COI") of the potential conflict. See Section 14 for details regarding Conflicts of Interest Regulations & Guidance: 42 CFR §50.603; 42 CFR §50.606(a); FDA 21 CFR §50.606(a); 21 CFR §54.1; 21 CFR §54.2; 21 CFR §54.4; 21 CFR §312.64(d); 21 CFR §812.110(d); 45 CFR §690; AAHRPP III.1.A.

3.8.7 Significant New Findings

During the course of Research, significant new knowledge or findings about the medication or Test Article and/or the condition under study may develop. The PI must report any significant new findings to the IRB and the IRB will review such findings with regard to potential impact on
the subjects’ rights and welfare. Since the new knowledge or findings may affect the risks or benefits to subjects or subjects’ willingness to continue in the Research, the IRB may require, during the ongoing review process that the PI contact the currently enrolled subjects to inform them of the new information. The IRB will communicate this to the PI. The informed consent should be updated and the IRB may require that the currently enrolled subjects be re-consented, acknowledging receipt of this new information and for affirming their continued participation.

Regulations & Guidance: OHRP Guidance on Written IRB Procedures; OHRP Guidance on Continuing Review; FDA Information Sheets: Continuing Review After Study Approval; AAHRPP II.2.D.

3.8.8 Advertisements

The IRB must approve any and all recruitment materials and/or advertisements prior to posting and/or distribution for studies that are conducted under the purview of the Institutional IRB. The IRB will review:

1. The information contained in the advertisement;
2. The mode of its communication;
3. The final copy of printed advertisements, prior to posting; and
4. The final audio/video taped advertisements,

This information should be submitted to the IRB with the Initial Application Form (TU Form 102) or as an amendment request to the Protocol along with the submittal.

The IRB reviews the material and the Advertisement Reviewer Checklist (TU Form 501) to assure that the material is accurate, and not coercive or unduly optimistic, creating undue influence to the subject to participate which includes, but is not limited to:

1. Statements implying a certainty of favorable outcome or other benefits beyond what was outlined in the consent document and the Protocol;
2. Claims, either explicitly or implicitly, that the Drug, Biologic or Device was safe or effective for the purposes under investigation;
3. Claims, either explicitly or implicitly, that the Test Article was known to be equivalent or superior to any other Drug, Biologic or Device;
4. Using terms like “new treatment,” “new medication,” or “new drug;”
5. Promising “free medical treatment” when the intent was only to say Participants will not be charged for taking part in the investigation;
6. Emphasis on payment or the amount to be paid, such as bold type or larger font on printed media; or
7. The inclusion of exculpatory language.

Advertisements will not include compensation for participation in a trial offered by a sponsor to involve a coupon good for a discount on the purchase price of the product once it has been approved for marketing.
Any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest. When appropriately worded, the following items may be included:

1. The name and address of the PI and/or Research facility;
2. The condition being studied and/or the purpose of the Research;
3. In summary form, the criteria that will be used to determine eligibility for the study;
4. The time or other commitment required of the subjects;
5. The location of the Research and the person or office to contact for further information;
6. A clear statement that this is Research and not treatment;
7. A brief list of potential benefits (e.g. no cost of health exam); or
8. IRB project number, the date of original IRB approval, and the date of IRB approval of the advertisement.

Once approved by the IRB, an advertisement cannot be altered or manipulated in any way without prior IRB approval.

Regulations & Guidance: DHHS 45 CFR §46.111(a)(3); 45 CFR §46.116; FDA 21 CFR §50.20; 21 CFR §56.111(a)(3); AAHRPP II.5.B.

### 3.8.9 Payment to Research Subjects

Payment to Research subjects may be an incentive for participation or a way to reimburse a subject for time, travel, parking, and other expenses incurred due to participation. However, payment for participation is not considered a Research benefit. Regardless of the form of remuneration, Investigators must take care to avoid coercion of subjects. Payments should reflect the degree of risk, inconvenience, or discomfort associated with participation. The amount of compensation must be proportional to the risks and inconveniences posed by participation in the study.

Investigators who wish to pay Research subjects must indicate in their Research project application the justification for such payment. Such justification should:

1. Substantiate that proposed payments are reasonable and commensurate with the expected contributions of the subject;
2. State the terms of the subject participation agreement and the amount of payment in the Consent Form (TU Forms 402; 403; and 407); and
3. Substantiate that subjects payments are fair and appropriate, and that they do not constitute (or appear to constitute) undue pressure on the subject to volunteer for the Research study.

The IRB must review both the amount of payment and the proposed method of disbursement to assure that neither entails coercion or undue influence.

The IRB does not allow the entire payment to be contingent upon completion of the entire study. As such, credit for payment should accrue and not be contingent upon the Participant completing the entire study. Any amount paid as bonus for completion of the entire study should not be so great that it becomes coercive.
The *Consent Form* (TU Forms 402; 403; and 407) must describe the terms of payment and the conditions under which subjects would receive partial payment or no payment (e.g., if they withdraw from the study before their participation is completed).

Unless the study is confidential, the University requires identifying information to issue checks, cash, or gift certificates to subjects. The *Consent Form* (TU Forms 402; 403; and 407) should inform subjects that they will be asked to provide their Social Security Number and verification of U.S Citizenship or Permanent Resident Status to receive payment, as applicable. For confidential studies, only names and addresses are required by the ORA, but the PI must keep an identity key in a secure place.

### 3.8.10 Tulane Employees:

University employees who participate in Research under the purview of Tulane’s IRB must be aware of the following:

1. Employees must disclose to the Research staff their employment status;
2. Attendance of study visits must be during off time, during annual time or on lunch (i.e., break time may not be used); and
3. Disclosure of the employees’ participation in a clinical trial may be made to your Department/Unit Head or Manager.

### 3.8.11 Recruitment Incentives

Payment arrangements among Sponsors, organizations, Investigators, and those referring Research Participants may place Participants at risk of coercion or undue influence or cause inequitable selection. Payment in exchange for referrals of prospective Participants from Researchers (physicians) (“finder’s fees”) is not permitted and may be considered illegal under Federal or State law. Similarly, payments designed to accelerate recruitment that is tied to the rate or timing of enrollment (“bonus payments”) also is not permitted. PIs are strongly encouraged to consult with Tulane’s OGC if they have any questions or concerns about recruitment incentives.

### 3.9 Compliance with all Applicable Laws and Regulations

The IRB follows and adheres to all applicable Federal, State and local laws in the jurisdictions where the Research is being carried out. The HRPO and Tulane’s IRB rely on the University’s OGC for interpretation and application of Federal and State law and the laws of any other jurisdiction where Research is conducted as they apply to Human Subject Research.

All consent forms also must be consistent with applicable State and local laws.

### 3.10 Possible IRB Actions

The IRB or reviewer(s) may arrive at the following decisions:

- Approval (or “Approve” or “Approved”) – see Section 3.10.1;
- Deferred with Minor Modifications—see Section 3.10.2;
- Deferred with Major Modifications—see Section 3.10.3;
- Disapproval (or (“Disapprove” or “Disapproved”)—see Section 3.10.4;
- Approval in Principal—see Section 3.10.5;
- Suspension or Termination—see Section 3.11.1; and
The following Sections provide clarification with respect to each of these decision options.

### 3.10.1 Approval:

**Approved (or “Approved,” “Approval,” or “IRB Approval”):** means the determination by the IRB that the investigation and Protocol, as submitted, has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and other institutional and Federal regulations. The Research may begin as of the IRB approval date. [DHHS 45 CFR §46.102(h); FDA 21 CFR §56.103(m)]. IRB Approval letters are automatically generated by IRBNet.

### 3.10.2 Deferred with Minor Modifications:

#### 3.10.2.1 Definitions

**Deferred with Minor Modification:** is a situation where the IRB cannot approve the Research as submitted or where the Proposal and/or Consent Form (TU Forms 402; 403; and 407) require minor revisions (e.g., wording changes, with replacement language provided). For Proposals submitted for Convened IRB Review, the needed revisions are agreed upon at the IRB meeting. For Proposals submitted Expedited Review, the needed revisions are designated by the reviewer(s). None of the required modifications can be related to the regulatory criteria for approval. These revisions are presented to the PI for incorporation by simple concurrence. Revisions must be made exactly as designated by the IRB or reviewer(s).

#### 3.10.2.2 Policy

An IRB decision to Defer with Minor Modifications includes situations where the IRB cannot approve the Research as submitted and where the Proposal and/or Consent Form (TU Forms 402; 403; and 407) require minor revisions (e.g., wording changes, with replacement language provided). For Proposals submitted for Convened IRB Review, the needed revisions are agreed upon at the IRB meeting. For Proposals submitted Expedited Review, the needed revisions are designated by the reviewer(s). None of the required modifications can be related to the regulatory criteria for approval. These revisions are presented to the PI for incorporation by simple concurrence. Revisions must be made exactly as designated by the IRB or reviewer(s).

In order to receive approval for a Protocol Deferred with Minor Modifications:

- For Proposals initially submitted for Convened IRB Review, the PI’s response, the revised Proposal and the previously submitted Proposal is given to the IRB Chair, HRPO Director, and/or a designee of the IRB for review. The reviewer(s) may approve the study upon receipt and approval of the revisions without further action by the IRB.

- For Proposals initially submitted for Expedited Review, the PI’s response, the revised Proposal and the previously submitted Proposal is given to the same reviewer(s) for review.

Approval of the Protocol application will not be granted and certification will not be issued until all deficiencies, if any, are corrected to the satisfaction of the IRB or the reviewer(s).
The outcome of the IRB’s deliberations or reviewer(s) findings is communicated to the PI in writing, which notice shall be issued within **10 working days** of determination. The PI may not proceed with the Research until receipt of notice of IRB/reviewer(s) approval of the Research.

The IRB’s determination concerning the revision will be documented in the minutes of the next regularly scheduled IRB meeting or in the IRB file for Expedited Review.

IRB Deferred with Minor Modification letters are automatically generated by IRBNet.

**3.10.3 Deferred with Major Modifications:**

**3.10.3.1 Definitions**

*Deferred with Major Modification:* is a situation where the IRB cannot approve the Research as submitted because (1) the Proposal and/or **Consent Form** (TU Forms 402; 403; and 407) require major modification or clarification; or (2) insufficient information is provided to adequately judge the Protocol application (e.g., the risks and benefits cannot be assessed with the information provided). IRB approval of the proposed Research must not occur until subsequent review of the material the PI submitted by the convened IRB or the expedited reviewer(s).

**3.10.3.2 Policy**

This IRB action is taken if major modification or clarification is required, or insufficient information is provided to adequately judge the Protocol application (e.g., the risks and benefits cannot be assessed with the information provided). IRB approval of the proposed Research must not occur until subsequent review of the material the PI submitted by the convened IRB or the expedited reviewer(s).

For Proposals initially submitted for Convened IRB Review, in order to receive approval for a Protocol Deferred with Major Modifications, the Investigator’s response must be submitted for review at a subsequent, convened meeting of the IRB. The HRPO provides the IRB with the PI’s response, the revised Proposal and the previously submitted Proposal. The item is placed on the agenda for re-review at the next meeting.

For proposals submitted for Expedited Review, in order to receive approval for the Protocol Deferred with Modifications, the Investigator’s response must be submitted for review.

IRB approval of the Proposal will not be granted and an approval letter will not be issued until all deficiencies, if any, are corrected to the satisfaction of the IRB or the reviewer(s).

The IRB’s determination concerning the subsequent amended Proposal will be documented in the minutes of the IRB meeting or in the file for Expedited Review. The outcome of the IRB action is communicated to the PI in writing through a letter via IRBNet.

**3.10.3.3 Time Limit for Submitting Requested Changes for New Research Protocol Application Deferrals (minor or major modifications)**

Failure to submit a response to IRB stipulated changes or inquiries related to new Research Protocols Deferred for Major or Minor Modifications within **90 days** will result in deactivation of the new Research Protocol application. The PI will receive written notification of the closure of the IRB file including an explanation for this action. PIs wishing to re-open their file must re-apply to the IRB following procedures outlined in this document. An extension beyond 90 days may be granted by the IRB if sufficient cause is provided by the PI. After the 90-day deadline, the IRB Program Coordinator will send E-mail notification of the time lapse to the PI requesting
a withdrawal of the study application. If changes or E-mail notification of the circumstances surrounding the delay are not received by the IRB Program Coordinator within one week of issuance of this notice, the study may be withdrawn by the IRB Program Coordinator.

3.10.4 Disapproved

The IRB action of Disapproved means that it cannot approve the Protocol as written. The IRB has determined that the Research cannot (1) be conducted on Institutional or TUHC premises, or other facilities; (2) cannot involve University or TUHC patients; (3) be conducted on or by Institutional employees or Institutional Agents; and/or be conducted under the auspices of Tulane’s IRB. Written notice of Disapproval will be issued by the IRB through IRBNet.

3.10.5 Approved in Principle

Approved in Principle is IRB approval, as requested by a Sponsor, without the IRB having reviewed all of the study procedures and consent documents. [DHHS 45 CFR §46.118]. There are two circumstances in which the IRB may grant approval required by a sponsoring agency without having reviewed all of the study procedures and consent documents. [45 CFR §46.118] One is if study procedures are to be developed during the course of the Research, but Human Subject approval is required by the sponsoring agency. The other is if the involvement of Human Subjects depends on the outcomes of work with animal subjects. The IRB may then grant approval without having reviewed the undeveloped recruitment, consent, and intervention materials. However, if the Proposal is funded, the PI must submit such materials for approval at least 60 days before recruiting Human Subjects into the study, or into any pilot studies or pre-tests. Approval in Principle is granted to satisfy sponsoring agency requirements or to allow Investigators to have access to funding to begin aspects of the project that do not involve Human Subjects. Approval in Principle may be done via Expedited Review.

3.11 Study Suspension, Termination and Investigator Hold

3.11.1 Suspension or Termination

IRB approval may be Suspended or Terminated if Research is not being conducted in accordance with IRB or regulatory requirements or has been associated with unexpected problems or serious harm to subjects. (See Section 8 for a discussion of Unanticipated Problems and Section 10 for a discussion of non-compliance)

Suspension of IRB approval is a directive of a convened IRB, IRB Chair(s) or HRPO Director to temporarily stop either some or all previously approved Research activities to ensure protection of the rights and welfare of study Participants or for non-compliance. Suspension directives made by the IRB Chair or HRPO Director must be reported to a meeting of the convened IRB. Suspended Protocols remain open and require Continuing Review.

Termination of IRB approval is a directive of the convened IRB to permanently stop some or all activities in a previously approved Research Protocol. If all Research activities are Terminated, the Research no longer requires Continuing Review.

The IRB shall notify the PI in writing of such Suspensions or Terminations and shall include an explanation of the reasons for the decision. The PI shall be provided with an opportunity to respond in person or in writing.

When a study is Suspended or Terminated, the convened IRB or authorized individual will:
1. Have any unanticipated problems reported to the IRB;
2. Consider actions to protect the rights and welfare of subjects;
3. Consider whether procedures for withdrawal of enrolled subjects take into account their rights and welfare; and
4. Consider informing current subjects of the Suspension or Termination.

All Suspensions or Terminations must be reported to the IO and reporting agency.

Suspension or Termination of Research approved that involves an IRB-approved Protocol also can be issued by University officials acting outside of an unrelated to the HRPP (i.e., not necessarily related to protecting the rights and welfare of study Participants). Such University actions can be made by the University President, Provost, Dean of the School of Medicine and Dean for the School of Public Health and Tropical Sciences. Such University actions may be made for any reason in furtherance of the Institution’s interest provided, however, that the aggrieved PI is entitled to all rights and procedures afforded to him/her under the Grievance Policy.

Regulations & Guidance: DHHS 45 CFR §46.113; FDA 21 CFR §56.113; AAHRPP II.4.D.

3.11.2 Investigator Hold

A PI or Sponsor may request an Investigator Hold on a Protocol when the PI/Sponsor wishes to temporarily or permanently stop some or all approved Research activities. Investigator Holds are not Suspensions or Terminations.

3.11.2.1 Procedures

PIs must notify the IRB in writing:

- Providing a description of the Research activities that will be stopped;
- Describing proposed actions to be taken to protect current Participants; and
- Describing actions that will be taken prior to IRB approval of proposed changes in order to eliminate apparent immediate harm.

Upon receipt of written notification from the PI, the IRB Program Coordinator places the Research study on the agenda for review. The IRB Chair, HRPO Director or HRPO Assistant Director, in consultation with the PI, determines whether any additional procedures need to be followed to protect the rights and welfare of current Participants as described in “Protection of Currently Enrolled Participants” below in Section 3.11.3.

The IRB Chair and/or HRPO Director, in consultation with the PI, determine how and when currently enrolled Participants will be notified of the administrative hold.

PIs may request a modification of the administrative hold by submitting a request for a modification to previously approved Research.

3.11.3 Protection of Currently Enrolled Participants

Before an investigator hold, Termination, or Suspension is put into effect, the convened IRB, IRB Chair (or designee) considers whether any additional procedures need to be followed to protect the rights and welfare of current Participants. Such procedures might include:
1. Transferring Participants to another PI;
2. Making arrangements for clinical care outside the Research;
3. Allowing continuation of some Research activities under the supervision of an independent monitor;
4. Requiring or permitting follow-up of Participants for safety reasons;
5. Requiring AEs or outcomes to be reported to the IRB and the Sponsor;
6. Notification of current Participants; and/or
7. Notification of former Participants.

3.12 Continuing Review

The IRB will conduct a continuing review (“Continuing Review”) of ongoing Research at intervals that are appropriate to the level of risk for each Research Protocol, but not less than once per year. Continuing Review must occur as long as the Research remains active for long-term follow-up of Participants, even when the Research is permanently closed to the enrollment of new Participants and all Participants have completed all Research-related interventions. Continuing Review of Research must occur even when the remaining Research activities are limited to the analysis of private identifiable information.

Regulations & Guidance: DHHS 45 CFR §46.109(e); FDA 21 CFR §56.109(f).

3.12.1 Approval Period

At Tulane, determination of the approval period and the need for additional supervision and/or participation is made by the IRB on a Protocol-by-Protocol basis. For example, for an Investigator who is performing particularly risky Research, or for an Investigator who has recently had a Protocol Suspended by the IRB due to regulatory concerns, an on-site review by a subcommittee of the IRB might occur or approval might be subject to an audit of study performance after a few months of enrollment, or after enrollment of the first several subjects.

For each initial or continuing approval the IRB will indicate an approval period with an approval expiration date specified. IRB approval is considered to have lapsed at midnight on the expiration date of the approval. For a study approved by the convened IRB, the approval period starts on the date that the IRB conducts its final review of the study; that is, the date that the convened IRB approved the Research or the date the convened IRB Deferred the Research for minor issues. For a study approved under Expedited Review, the approval period begins on the date the IRB Chair or IRB member(s) designated by the IRB Chair gives final approval to the Protocol.

The approval date and approval expiration date are noted on initial approvals and subsequent Continuing Review approvals sent to the P.I. and must be strictly adhered to. Investigators should allow sufficient time for development and review of renewal submissions.

Review of a change in Research ordinarily does not alter the date by which Continuing Review must occur. This is because Continuing Review is review of the full Protocol, not simply a change to it.

The regulations make no provision for any grace period extending the conduct of Research beyond the expiration date of IRB approval. Therefore, Continuing Review and re-approval of
Research must occur by midnight of the date when IRB approval expires. If the IRB performs Continuing Review within 30 days before the IRB approval period expires, the IRB may retain the anniversary date as the date by which the Continuing Review must occur.

3.12.2 Continuing Review Process

To assist PIs, IRBNet generates courtesy reminders to Investigators 90 days and 60 days in advance of the study expiration date so that they timely submit Continuing Reviews. PIs must submit Continuing Reviews electronically via IRBNet. It is the PI’s responsibility to ensure that the Continuing Review of ongoing Research is approved prior to the expiration date. By Federal regulation, no extension to that date can be granted.

Information and documentation to be uploaded by PIs into IRBNet includes the following:

- The Application for Continuing Review (TU Form 603) with redline edits (i.e., changes are to be highlighted, deletions are to be lined through) to reflect any changes from the prior submission;
- The current Consent Form (TU Forms 402; 403; and 407);
- Any newly proposed Consent Form document with redline edits (i.e., changes are to be highlighted, deletions are to be lined through) to reflect any changes from the prior submission;
- The full Protocol or a Protocol summary containing the relevant information necessary to determine whether the proposed Research continues to fulfill the criteria for approval;
- A status report on the progress of the Research that includes:
  - A summary since the last IRB review of:
    - Unanticipated Problems Involving Risks to Participants or Others;
    - AEs, untoward events, and adverse outcomes experienced by Participants.
    - Participant withdrawals;
    - The reason for withdrawals;
    - Complaints about the Research;
    - Amendments or modifications;
    - Any relevant recent literature; and
    - Any interim findings.
- Any relevant multi-center trial reports;
- The consent form of the last two patients that was on the study with adapted identifying information removed or blacked out.
- The Investigator’s current risk-potential benefit assessment based on study results;
- The gender and minority status of those entered into the Protocol, including:
  - Number of Participants considered as members of specific Vulnerable Populations; and
An assurance that all serious and unexpected AEs had been reported as required.

- Application for Continuing Review (TU Form 603);
- HIPAA Authorization Form (TU Form 405);
- Delegation of Authority (TU Form 1001);
- FDA Form 1572s, if applicable; and
- Non-Prompt Report Form for submission of anticipated problems or events that have been described in the Protocol, Consent Form (TU Forms 402;403; and 407) and/or Investigator’s brochure that have occurred.

In conducting Continuing Review of Research not eligible for Expedited Review, all IRB members will be directed to review the above materials along with all prior materials uploaded into IRBNet. At the meeting, the primary (and secondary reviewers for the Biomedical IRB) lead the IRB through the completion of the regulatory criteria for approval in the Continuing Review Reviewer Sheet (TU Form 504).

After the Convened IRB Meeting, primary and secondary reviewers must complete the Deferred MAJOR Continuing Review Reviewer Sheet (TU Form 515) or Deferred MINOR Continuing Review Reviewer Sheet (TU Form 516), as appropriate, if the IRB recommended deferring IRB approval.

The HRPO staff attends the convened meetings and ensures that the complete Protocol files for each Protocol on the agenda have been uploaded into IRBNet. The HRPO staff will retrieve any additional materials should the IRB members or reviewer(s) request.

In the case of Expedited Reviews, the IRB members may request the HRPO staff to provide them with additional materials required for the review.

Review of currently approved or newly proposed consent documents must occur during the scheduled Continuing Review of Research by the IRB. However, informed consent documents should be reviewed whenever new information becomes available that would require modification of information in the IRB-approved informed consent document. Changes to consent documents are amendments and will be reviewed according to the procedures in Section 3.13.

**Continuing Review of a study must continue until:**

- The Research is permanently closed to the enrollment of new Participants;
- All Participants have completed all Research-related interventions; and
- Collection and analysis or private identifiable information has completed

**3.12.3 Expedited Review of Continuing Review**

In conducting Continuing Review under Expedited Review, the reviewer(s) shall have access to all of the above materials specified in Section 3.12.2. The reviewer(s) complete the Continuing Review Reviewer Sheet (TU Form 504) to determine whether the Research meets the criteria allowing Continuing Review using the Expedited Review procedure, and, if so, whether the Research continues to meet the regulatory criteria for approval.
Generally, if Research did not qualify for Expedited Review at the time of Initial Review, it does not qualify for Expedited Review at the time of Continuing Review, except in limited circumstances described by Expedited Review Paragraphs (8) and (9) found in Section 3.5.1 (Expedited Review Categories). [See 63 FR 60364-60367]. It is also possible that Research activities that previously qualified for Expedited Review in accordance with 45 CFR §46.110, have changed or will change, such that Expedited Review would no longer be permitted for Continuing Review.

3.12.4 Lapse in Continuing Review Approval

The regulations permit no grace period or approval extension after approval expiration. Research that continues after the approval period has expired is considered to be Research conducted without IRB approval. If the Continuing Review approval does not occur within the timeframe set by the IRB, this is a lapse in Continued Review approval. All Research activities must stop. This includes cessation of subject recruitment (e.g., media advertisements must be pulled), enrollment, consent, interventions, interactions, and data collection, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the Research interventions or interactions. This will occur even if the Investigator has provided the required information for continued review before the expiration date. Therefore, Investigators must allow sufficient time for IRB review and approval.

It is the responsibility of the PI to ensure that a lapse in approval does not occur. The HRPO will notify the PI of the expiration of approval and that all Research activities must cease.

If Research Participants are currently enrolled in the Research project and their participation is ongoing, once notified of the expiration of approval, the PI must immediately submit to the IRB Chair a list of Research subjects for whom Suspension of the Research would cause harm. Enrollment of new subjects cannot occur and continuation of Research interventions or interactions for already enrolled subjects will only continue when either the IRB, IRB Chair, or HRPO Director, upon consultation with the IO, finds that it is in the best interest of the individual subjects to do so.

Failure to timely submit Continuing Review information is considered Non-Compliance by the PI and will be handled according to the Non-Compliance policy (See Section 10.4).

Once approval has expired (i.e., lapse in Continuing Review approval), IRB review and re-approval must occur prior to re-initiation of the Research. If the study approval has lapsed more than 30 days and the PI has not submitted an Application for Continuing Review (TU Form 603), the study will be closed by the IRB.

If the IRB requires revisions to obtain Continuing Review approval and no response has been received from the PI within 60 days following IRB correspondence, the study will be closed unless the IRB determines that study closure will harm subjects.

3.13 Amendment of an Approved Protocol.

PIs who wish to modify or amend their approved applications must seek IRB approval before making any changes in approved Research. This requirement exists even though the changes are planned for the period for which IRB approval has already been given. One noteworthy exception are for changes necessary to eliminate an immediate hazard to the subject, in which case the IRB must then be notified at once).
Amendments may be approved if they are within the scope of what the IRB originally authorized. For example, if a Researcher wishes to add a population to an existing study, but not alter the study procedures or purpose, an amendment request is usually appropriate. Likewise, amending a procedure without changing the study's purpose or study population may also be appropriate. If, however, the Researcher wishes to add a population and revise study procedures, he or she will need to submit a new application for Human Subjects approval.

Investigators must submit documentation to inform the IRB about the changes in the status of the study. To this end, Investigators are required to submit the changes through the modification/Amendment package in IRBNet:

- Completed Application for Amendment (TU Form 601);
- Revised Sponsor’s Protocol (if applicable);
- Revised approved Consent (TU Forms 402, 403)/Assent (TU For 401) documents (if applicable) or other documentation that would be provided to subjects when such information might relate to their willingness to continue to participate in the study;
- Revised or additional recruitment materials; or
- Any other relevant documents provided by the Investigator

HRPO staff or HRPO Director will determine whether the proposed changes may be approved through an Expedited Review process, if the changes are minor, or whether the amendment warrants Convened IRB Review. The reviewer(s) using the Expedited procedure has the ultimate responsibility to determine that the proposed changes may be approved through the Expedited Review procedure and, if not, must refer the Protocol for Convened IRB Review.

Regulations & Guidance: AAHRPP II.2.E; OHRP Guidance on Written IRB Procedures.

3.13.1 Expedited Review of Protocol Amendments/Modifications

An IRB may use Expedited Review procedures to review minor changes in ongoing previously-approved Research during the period for which approval is authorized. An Expedited Review may be carried out by the IRB Chair and/or designee(s) among the IRB members.

The reviewer(s) complete the Amendment Reviewer Sheet (TU Form 503) to determine whether the modifications meet the criteria allowing review using the Expedited procedure, and if so, whether the Research with the proposed modifications continues to meets the regulatory criteria for approval.

The reviewer will also consider whether information about those modifications might relate to Participants’ willingness to continue to take part in the Research and if so, whether to provide that information to Participants.

3.13.2 Convened IRB Review of Protocol Modifications

When a proposed change in a Research study is not minor (e.g., procedures involving increased risk or discomfort are to be added), then the IRB must review and approve the proposed change at a convened meeting before the change can be implemented. The only exception is a change necessary to eliminate apparent immediate hazards to the Research subjects. In such a case, the IRB should be promptly informed of the change following its implementation and should review the change to determine that it is consistent with ensuring the subjects' continued welfare.
All documents provided by the PI are accessible to all IRB members via IRBNet.

At the meeting, the Primary Reviewer presents an overview of the modifications and leads the IRB through the completion of the regulatory criteria required for approval. The IRB will determine whether the Research with the proposed modifications continues to meet the regulatory criteria for approval.

When the IRB reviews modifications to previously approved Research, the IRB consider whether information about those modifications might relate to Participants’ willingness to continue to take part in the Research and if so, whether to provide that information to Participants.

3.13.3 Changes in the Informed Consent Document

When a modification makes it necessary to change the informed consent document, regardless of whether any Participants are enrolled, two copies of the revised consent document are to be submitted to the IRB. One “mark up” copy should show all changes from the previous version (i.e., highlighting all additions and striking through all deletions). The one clean copy will contain the IRB – approval stamp without any outdated text.

3.14 Closure of Protocols

The completion or Termination of a study is a change in activity that must be reported by the PI to the IRB on the Application for Closures (TU Form 602). Although subjects will no longer be at risk under the study, a final report to the IRB allows it to close the study in IRBNet as well as provide information that may be used by the IRB in the evaluation and approval of related studies involving the PI.

The PIs should submit the Application for Closures (TU Form 602) through IRBNet. The PI must submit a final report with the closure application. IRB staff will review the closure application for completeness utilizing the Administrative Reviewer Sheet for Study Closures (TU Form 514) and will notify the IRB. Closure applications in which the Protocol will expire prior to the next scheduled IRB meeting will be closed and the final report will be included on the next agenda as a “Closure” item. Closure applications in which the expiration date of the Protocol is after the next scheduled meeting will be placed on the agenda as a “Closures” item and closed effective the date of the meeting.

3.15 Notice to PI of IRB Actions

Barring extraordinary circumstances, all IRB action letters are prepared by HRPO staff and are uploaded via IRBNet for review by the Principal Investigator (PI) and research team within ten (10) working days. For an approval, along with written notification of approval, a copy of the approved Consent (TU Forms 402, 403)/Assent (TU Form 401) document(s) containing the stamped approval with the dates of the approval and expiration on each sheet will be uploaded. For required modifications or deferrals, the notification will include the information that is required, the basis for requiring those modifications, and a deadline for response submission. For a disapproval, termination or suspension, the notification will include the basis for making that decision.

All correspondence between IRB and investigators are retained in IRBNet.

The IRB reports its findings and actions to the Institution in the form of its minutes, a copy of which is distributed by IRB staff to IO with a copy stored in the HRPO files.
3.16 Appeal of IRB Decision to Disapprove

When an IRB Protocol presented at a convened meeting is Disapproved, Deferred with Minor Modification, or Deferred with Major Modification, the IRB will notify the PI in writing about the specific deficiencies and the modifications that are necessary for appropriate IRB approval. The IRB shall include in its written notification a statement of the reasons for its decision and give the PI an opportunity to respond in writing. The PI also is given the opportunity to schedule a meeting with the IRB to discuss this matter.

In cases where there is disagreement between the IRB and the PI regarding the nature and extent of the requested changes and these disagreements cannot be resolved amicably in an informal manner, the PI and/or the IRB may make an appeal to the IO for a resolution of the matter. The IO may organize a meeting to help facilitate discussion between the IRB and the PI. While the IO may provide input and make recommendations to the IRB for expeditious resolution of the matter, final recommendations for approval remain under the purview of the IRB.

Regulations & Guidance: DHHS 45 CFR §46.109(d); FDA 21 CFR §56.109(e).

3.17 National Cancer Institute's Central IRB

3.17.1 Adult and Pediatric Initiatives

Tulane is a Participant in the National Cancer Institute’s (“NCI”) Central Institutional Review Board (“CIRB”) Initiative. Local PIs who wish to enroll patients in CIRB-approved Protocols are encouraged to utilize this service for adult and pediatric cancer trials. NCI requires that PIs wishing to use a CIRB must first submit CIRB review materials and locally required materials to the IRB for a facilitated review by one member, who will review the acceptability of CIRB as the IRB-of-record for that particular study. Such PIs should first contact the HRPO Director (or designee) to complete paperwork to secure a username and password for the PI and study coordinator.

3.17.2 PIs wishing to utilize an NCI CIRB must:

1. Submit a Protocol package that contains:
   - The CIRB Submission Sheet (TU Form 103) with respect to facilitated IRB review of NCI CIRB-approved studies;
   - The TUHC Approval Form, downloaded from TUHC’s Website;
   - The CIRB Application, Protocol, notification letters, Unanticipated Problem Reports and amendments, downloaded from the CIRB Website;
   - A CIRB-approved Consent Form (TU Forms 402; 403; and 407), modified in accordance with our local boilerplate language required by Tulane in its consent forms, as well as a HIPAA Privacy section, and contact information.

   NOTE: NCI has strict rules regarding what modifications can be made to a CIRB-approved consent document. Impermissible changes include deletions of any information from the document. Permitted changes include (1) minor word substitutions or additions to the Consent Form (TU Forms 402; 403; and 407), to conform to, for example, Institutional requirements or IRB policies, or to clarify statements, as long as the changes
don’t alter the meaning of the CIRB-approved contents; or (2) additional risks as deemed necessary as a result of facilitated review.

1. The HRPO Director (or designee) will upload the remaining CIRB documentation (i.e., CIRB reviews, minutes etc.), relevant to the study being submitted locally for review.

2. The IRB Chair (or designated IRB member(s)) will conduct a facilitated review of the downloaded documents. There are three possible outcomes, relayed to the PI by way of IRBNet:

   • Approved (for CIRB Oversight): The CIRB will be designated as the IRB-of-record. You will receive an acceptance letter, a copy of the confirmation E-mail from the CIRB, and a hard copy of the local consent document(s).

   • Modifications required (in order to secure approval for CIRB Oversight): Specific stipulations must be addressed before the CIRB can be designated as the IRB-of-record. See Consent Form (TU Forms 402; 403; and 407) issue above, and:

   • Protocol not accepted (for CIRB Oversight): Local IRB oversight is required. You must complete a local IRB application and submit materials to the HRPO via the standard application process. The CIRB will not be permitted to oversee the Protocol.

3.17.3 When a Protocol has been Approved for CIRB Oversight

1. HRPO Director (or designee) notifies CIRB (via the CIRB Website) and the PI (via IRBNet), the PI will upload stamped consent documents into IRBNet for use by the PI and Research team.

2. Once the CIRB is designated as the IRB-of-record for a study, PI’s interaction with the HRPO and IRB includes:

   • Consent Form Revisions by CIRB: the PI must make all changes on the local consent/permission/assent form, update the header to match the CIRB-approved consent and upload into IRBNet for review and updated stamping by HRPO Director (or designee).

   • Continuing Reviews: Continuing Review will be conducted by the CIRB. All applicable CIRB paperwork should be uploaded into IRB Net, along with a copy of CIRB’s review for the study, the updated local consent form, and Tulane’s Continuing Review Application for NCI CIRB Studies. Materials will be reviewed and consents will receive updated stamping by HRPO Director (or designee).

   • Unanticipated Problems: must be submitted to the HRPO for all subjects enrolled through Tulane (“local UP’s”), in accordance with IRB policy.

   • Personnel Changes: Any local personnel changes, local advertisements etc. must be submitted to the HRPO for review and approval. Notification regarding review outcome (approval, modifications required etc) will be sent to PI.

   • Study Closure: To close a CIRB study with activity at a Tulane site, the PI must submit a Application for Closure (Form 602) to HRPO, who will, in turn, notify the CIRB.
4 Documentation and Records

4.1 Policy
The University shall prepare and maintain adequate documentation of the IRB(s) activities. All records must be accessible for inspection and copying by authorized representatives of the FDA, OHRP, Sponsors, and other authorized entities at reasonable times and in a reasonable manner.

4.2 Definitions

Research Records (or “Investigator Records”): consists of records (as well as Case Histories or any data) prepared, created, gathered, or maintained by a PI, Investigator or research staff for Research Under the Auspices of the Institution.

Substantive: an action taken by an IRB that materially alters the substance and meaning of a Protocol, informed consent form or process, or Investigator status, including, but not limited to, Restriction, Suspension or Termination of a study or Investigator participation, and actions taken to prevent future occurrence(s) of the AE in Research.

4.3 IRB Records

IRB Records include, but are not limited to:

- Written operating procedures. (See Section 1.11).
- IRB membership rosters, (See Section 4.5).
- Training records. The IRB records coordinator maintains accurate records listing research investigators, IRB members, and IRB staff that have fulfilled the facility’s human subject training requirements. Electronic copies of documentation are maintained in the official IRB records located in the IRB Office.
- IRB correspondence (other than Protocol related).
- IRB Study Files (See Section 4.4 for information included in study files)
- Documentation of Emergency Exemption from Prospective IRB Approval.[FDA 21 CFR §56.104(c)]. (See Section 7.6).
- Documentation of Exceptions from Informed Consent Requirements for Emergency Use of a Test Article [(FDA 21 CFR §50.23]. (See Section 7.6).
- Documentation of exemptions (See Section 4.7).
- Documentation of Convened IRB meetings minutes (see Section 4.4 for information included in the minutes).
- Documentation of review by another institution’s IRB when appropriate.
- Documentation of cooperative review agreements, e.g. Memoranda of Understanding (MOUs).
- Federal Wide Assurances.
- Quality assurance reviews.
- IRB membership roster(s).
- IRB meeting minutes.

Documentation for off-site IRBs includes:

- On-line access to all applicable Protocol documents
- MOU/Agreements of IRB Services
Workflow/SOPs
Notes/documents pertaining to Tulane administrative reviews

Regulations & Guidance: DHHS 45 CFR §46.115(a)-(b); FDA 21 CFR §56.115(a)-(b); AAHRPP II.3.A.

4.4 IRB Study Files

HRPO will maintain an electronic study file for each IRB study submission that is submitted via IRBNet for review. Once a study submission is confirmed to include appropriate submission materials, and signature of PI and Department Chair, it is assigned a unique IRB number by HRPO and a unique IRBNet number.

All communications to and from the IRB are maintained. Depending on the type of communication, maintenance may be via IRBNet, HRPO staff E-mail, or paper. IRB study files include, but are not limited to:

1. Protocol and all other documents submitted as part of an initial IRB Application (TU Form 102).
2. Protocol and all other documents submitted as part of a request for Application for Continuing Review (TU Form 603)/Application for Closure (TU Form 602). This also includes progress reports, statements of significant new findings provided to Participants, reports of injuries to patients.
3. Documents submitted and reviewed after the study has been approved, including reports of modifications to Research/amendments and Unanticipated Problem reports.
4. Copy of the IRB-approved Consents (TU Forms 402, 403)/Assents (TU Form 401).
5. Sponsor-approved sample consent form document and Protocol, when they exist
6. IRB reviewer forms (when Expedited Review procedures are used)
7. Documentation of type of IRB review.
8. For Expedited Review, documentation of any determinations required by the regulations and Protocol-specific findings supporting those determinations, including: waiver or alteration of the consent process, research involving Pregnant Women, Fetuses, and Neonates, Research involving Prisoners, and Research involving Children.
9. Documentation of all IRB review actions.
10. Notification of expiration of IRB approval to the PI and instructions for submitting relevant continuing review materials.
12. Correspondence pertaining to appeals.
13. Copies of approval letters and forms that describe what PIs must have before beginning the study.
14. IRB correspondence to and from Investigators.
15. All other IRB correspondence related to the Research.
17. Documentation of audits, investigations, reports of external site visits.
19. DHHS-approved sample consent document and Protocol, when they exist.

Regulations & Guidance: FDA 21 CFR §56.115(a).

4.5 IRB Membership Roster

A membership list of IRB members must be maintained for each IRB committee. It must identify members sufficiently to describe each member's chief anticipated contributions to IRB deliberations. The list must contain the following information about IRB members:

1. Name;
2. Earned degrees;
3. Affiliated or non-affiliated status (neither the member nor an immediate family member of the member may be affiliated with the University);
4. Employment or other relationship between each IRB member and Tulane;
5. Status as scientist (physician-scientist, other scientist, non-scientist or social behavioral scientist). For purposes of this roster, IRB members with Research experience are designated as scientists (including the student member). Research experience includes training in Research (e.g., doctoral degrees with a Research-based thesis) and previous or current conduct of Research. Students being trained in Research fields will be designated as scientists;
6. Indications of experience, such as board certifications or licenses sufficient to describe each member's principal anticipated contributions to IRB deliberations;
7. Representative capacities of each IRB member; which IRB member is a Prisoner representative (as required by Subpart C of 45 CFR Part 46), and which IRB members are knowledgeable about or experienced in working with Children, Pregnant Women, cognitively-impaired individuals, and other Vulnerable Populations locally involved in Research;
8. Role on the IRB (e.g., IRB Chair, IRB Vice-Chair, etc.);
9. Voting status. Note that all IRB members are, by definition, entitled to vote. Guests and ex-officio guests do not have a right to vote or be counted toward a Quorum; and
10. Alternate Member status, including the IRB member for whom they alternate with.

The HRPO must keep the IRB membership list current. IRB Records include a curriculum vitae (“CV”), and education of each IRB member. The HRPO Director must promptly report changes in IRB membership to OHRP.

Regulations & Guidance: FDA 21 CFR §56.115(a).

4.6 The IRB Minutes

Actions by duly convened IRB proceedings must be reduced to writing and available for review and approval within 3 weeks of the recorded meeting date. Once approved by the IRB at a
subsequent IRB meeting, the minutes must not be altered by anyone including a higher Institutional authority. It should be noted that errors or corrections to approved IRB minutes, as approved by a majority of the Convened IRB, will be included in the next meeting minutes.

A copy of IRB-approved minutes for each IRB meeting will be distributed to the IO.

Minutes of IRB meetings must contain sufficient detail to show:

1. Names of IRB members present;
2. Names of IRB members or IRB Alternate Members who are participating through videoconference, teleconference or other electronic means, and documentation that those not physically present have received all pertinent material prior to the meeting and were able to actively and equally participate in all discussions;
3. Names of absent IRB members;
4. Names of alternates attending in lieu of specified (named) absent IRB members. Alternates may substitute for specific absent members only as designated on the official IRB membership roster;
5. Names of consultants present, if applicable;
6. Name of Investigators or Research staff present;
7. Names of guests present;
8. The initial attendance list shall include those members present at the beginning of the meeting. The minutes will indicate, by name, those members who enter or leave the meeting. The vote on each action will reflect those members present for the vote on that item;
9. The presence of a Quorum initially and throughout the IRB meeting, including the presence of one member whose primary concern is in a non-scientific area;
10. Business items discussed;
11. Continuing education conducted;
12. Actions taken, including separate deliberations, actions, and votes for each Protocol undergoing Initial Review, Continuing Review, or review of modifications by the convened IRB;
13. Votes on these actions (total number voting; number voting for; number voting against; number abstaining; number of those excused, number of those recused);
14. Basis or justification for all IRB actions and/or decisions including required changes in Research or disapproval;
15. Summary of controverted issues and their resolution;
16. Approval period for initial and continuing review Protocols, including identification of Research that warrants review more often than annually and the basis for that determination;
17. Risk level of initial and continuing review approved Protocols;
18. Review of interim reports (e.g. AEs or safety reports; amendments; report of violations or deviations, etc.);

19. Review of DSMB summaries;

20. Review of DSM plans;

21. Applications that have met or not met the stipulations;

22. Justification of deletion or Substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document;

23. Protocol-specific documentation that the Research meets the required criteria [45 CFR §46.116(d)] when approving a consent procedure that does not include or that alters some or all of the required elements of informed consent, or when waiving the requirement to obtain an informed consent;

24. Protocol-specific documentation that the Research meets the required criteria [45 CFR §46.117(c)] when the requirements for documentation of consent are waived;

25. When approving Research that involves populations covered by Subparts B, C, or D of 45 CFR §46, the minutes will document the IRB(s) justifications and findings regarding IRB determinations stated in the Subparts or the IRB(s) agreement with the findings and justifications as presented by the PI on IRB forms;

26. The rationale for SR Device/NSR Device determinations;

27. COI determinations;

28. Identification of any Research for which there is need for verification from sources other than the PI that no material changes are made in the Research (e.g., cooperative studies, or other collaborative Research);

29. Special protections warranted in specific Research projects for groups of subjects who are likely to be vulnerable to coercion or undue influence, such as Children, Prisoners, Pregnant Women, mentally-disabled persons, or economically- or educationally-disadvantaged persons, regardless of source of support for the Research;

30. A list of Research approved since the last meeting utilizing Expedited Review procedures and the specific citation for the category of Expedited Review of the individual Protocol;

31. Documentation of approval by the IRB Chair (or designee) of Research contingent on specific minor conditions in the minutes of the first IRB meeting that takes place after the date of the approval;

32. An indication that, when an IRB member has a COI (see Section 2.8) with the Research under review, the IRB member was not present during the deliberations or voting on the Proposal, and that the Quorum was maintained. The name of the IRB member will be captured in the minutes as well as the reason for their departure; and

33. Key information provided by consultants will be documented in the minutes or in a report provided by the consultant.

Regulations & Guidance: 45 CFR §46.116(c)-(d); 45 CFR §46.117(c); 45 CFR §46.204; 45 CFR §46.205; 45 CFR §46.206; 45 CFR §46.207; 45 CFR §46.305; 45 CFR §46.306; 45 CFR
§46.404; 45 CFR §46.405; 45 CFR §46.406; 45 CFR §46.407; 45 CFR §46.408; 42 USC 498 A(b)(1); 42 USC 498 A(b)(2); 42 USC 498 A(c); FDA 21 CFR §50.51; 21 CFR §50.52; 21 CFR §50.53; 21 CFR §50.54; 21 CFR §50.55; 21 CFR §50.56; 21 CFR §56.109(c); 21 CFR §56.115(a); AAHRPP II.3.A.; and II.3.C.

4.7 Documentation of Exempt Review Findings

Documentation of Exempt Review consists of the reviewer’s citation of a specific Exemption category and written concurrence by the IRB of the activity.

4.8 Documentation of Expedited Reviews

IRB Records for initial and Continuing Review by the Expedited procedure must include:

1. The specific permissible category;
2. A description of action taken by the reviewer;
3. The approval period; and
4. Any determinations required by the regulations including Protocol-specific findings supporting those determinations.

4.9 Access to IRB Records

The IRB has policies and procedures to protect the confidentiality of research information:

1. All paper IRB records are kept secure in locked filing cabinets or locked storage rooms. The HRPO is closed and locked when unattended.
2. IRBNet, Tulane’s electronic IRB web-based program, is hosted at an out-of-state, enterprise class, data facility. Facilities are secure, data is mirrored, and IRBNet’s data is backed up nightly to off-site fire-rated facilities. Authorized users have restricted access to the facility. Security precautions are state of the art. Security standards associated with user ids and passwords are in accordance with generally accepted commercial and federal security. Certified SSL (128 bit Secured Socket Layer technology) encryption is standard for all web-based transmissions. Strict permission rules ensure that only approved individuals have access to Tulane data.
3. Access to IRB records, whether paper or electronic, is limited to the IO, IRB Chair, IRB members, HRPO staff, authorized institutional officials, and officials of Federal and state regulatory agencies (OHRP, FDA). Research investigators are provided reasonable access to files related to their research. Appropriate accreditation bodies are provided access and may recommend additional procedures for maintaining security of IRB records. All other access to IRB records is limited to those who have legitimate need for them, as determined by the IO.
4. Records are accessible for inspection and copying by authorized representatives of Federal regulatory agencies during regular business hours.
5. Paper records may not be removed from the HRPO Office; however, the HRPO staff will provide copies of records for authorized personnel if requested.
6. All other access to IRB study files, paper or electronic, is prohibited.
4.10 Record Retention

IRB Records (as described in Section 4.3) pertaining to Research, which is conducted, must be stored securely. Paper records are stored in HRPO and electronically kept in IRBNet.

IRB Records must be retained for at least three (3) years after completion of the Research. IRB Records not associated with Research or for Protocols cancelled without Participant enrollment will be retained at the facility for at least 3 years after closure of the IRB file.

IRB Records retained beyond their retention date will be shredded or otherwise destroyed.

See Section 4.12.1 for record retention requirements for studies involving Investigational Drugs and Investigational Devices.

Regulations & Guidance: DHHS 45 CFR §46.115(b); FDA 21 CFR §56.115(b); 21 CFR §56.312.62(c); AAHRPP II.3.B.

4.11 Investigator Records

PIs are required to maintain accurate, current and complete records of their Human Subject Research activities. In general, PIs should establish and maintain a file for each study that has been reviewed by the IRB. These files should closely resemble the IRB’s file structure on the study.

Within each study, PIs also should maintain a file for each subject who signs a consent document agreeing to participate in the study. These subject-specific files should include the original signed consent document and copies of case report forms, and any other correspondence between the PI and the subject.

Research Records should be maintained as appropriate to the type of study. For example, when a study is Sponsored externally, these records should be kept for at least 3 years after the study has been completed and the Sponsor has indicated that the records are no longer required.

4.12 Records for FDA-Regulated Studies

4.12.1 Investigational Drugs

Investigators are expected to maintain accurate, complete and current records with respect to studies involving Investigational Drugs consistent with FDA requirements found at 21 CFR §312.62(a)(b)(c). This includes the following:

1. **Disposition of Drug:** A PI is required to maintain adequate records of the disposition of the Drug, including dates, quantity, and use by subjects.

2. **Case Histories:** A PI is required to prepare and maintain adequate and accurate Case Histories that record all observations and other data pertinent to the investigation on each individual Administered the Investigational Drug or employed as a control in the investigation. Case Histories include the case report forms and supporting data including (e.g., signed and dated consent forms), and medical records (e.g., physician progress notes, the individual’s hospital chart(s), and the nurses’ notes). The Case History for each individual shall document that informed consent was obtained prior to participation in the study.
3. **Record retention:** A PI shall retain records involving Investigational Drugs involved in an FDA-regulated study for a period of 2 years following the date a marketing application is approved for the Drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.

Regulations & Guidance: FDA 21 CFR §312.62.

### 4.12.2 Investigational Devices

PIs must maintain accurate, complete and current records involving Investigational Devices involved in an FDA-regulated study consistent with FDA requirements found at 21 CFR §812.140(a)(d). This includes the following:

1. All correspondence with another Investigator, an IRB, the Sponsor, a monitor, or FDA, including required reports;
2. Records of receipt, use or disposition of a Device that relate to:
   a. The type and quantity of the Device, the dates of its receipt, and the batch number or code mark.
   b. The names of all persons who received, used, or disposed of each Device.
   c. Why and how many units of the Device have been returned to the Sponsor, repaired, or otherwise disposed of.
3. Records of each subject’s Case History and exposure to the Device. Case Histories include the case report forms and supporting data (e.g., signed and dated consent forms) and medical records (e.g., physician progress notes, copies of individual’s hospital chart(s), and the nurses’ notes). Such records shall include:
   a. Documents, evidencing informed consent and, for any use of a Device by the Investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent. The Case History for each individual shall document that informed consent was obtained prior to participation in the study.
   b. All relevant observations, including records concerning Adverse Device Effects ADEs (whether anticipated or Unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
   c. A record of the exposure of each subject to the Investigational Device, including, the date and time of each use, and any other therapy.
4. The Protocol with documents showing the dates of and reasons for each Deviation from the Protocol.
5. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.
5 Obtaining Informed Consent from Research Subjects

5.1 Policy

No Investigator conducting Research Under the Auspices of the Institution may involve a Human Subject in Research without obtaining the legally effective informed consent of the subject or the subject’s Legally Authorized Representative unless a waiver of consent has been approved by the IRB in accordance with Section 5.9 of these procedures. Except as provided in Section 5.9, informed consent must be documented by the use of a written consent form approved by the IRB (See Section 5.7).

The IRB will evaluate both the consent process and the procedures for documenting informed consent to ensure that adequate informed consent is obtained from Participants.

The following procedures describe the requirements for obtaining consent from Participants in Research Under the Auspices of the Institution.

Regulations & Guidance: DHHS 45 CFR §46.116; FDA 21 CFR §50.20; AAHRPP II.7.A.

5.2 Basic Requirements

Informed consent must be obtained by the PI (or properly trained designee) prior to entering or enrolling a subject into an IRB-approved study and/or conducting any study related procedures required by the Protocol, unless consent is waived by the IRB.

If someone other than the PI conducts the interview and obtains consent from patient subject, the PI needs to formally delegate this responsibility, and the person so delegated must have received appropriate training to perform this activity. The person so delegated must be knowledgeable about the Research to be conducted and the consenting process, and must be able to answer questions about the study. The PI should complete, maintain and update the Log entitled Signature and Delegation Log (TU Form 1001).

These informed consent requirements are not intended to preempt any applicable Federal, State, or local laws that require additional information to be disclosed for informed consent to be legally effective.

Sample or draft consent documents may be developed by a Sponsor or cooperative study group. However, the IRB-of-record is the final authority on the content of the consent documents that is presented to the prospective study subjects.


5.3 Securing and Documenting Informed Consent

A PI is required to obtain legally effective informed consent from a subject or the subject’s Legally Authorized Representative. [DHHS 45 CFR §46.177; FDA 21 CFR §50.20; AAHRPP II.7.D]. When informed consent is required, it must be sought prospectively, and properly documented. [DHHS 45 CFR §46.117; FDA 21 CFR §50.20]. The requirement to obtain the legally effective informed consent of individuals before involving them in Research is one of the central protections provided for by the Federal regulations and the Tulane HRPP.

The informed consent process involves three key features: (1) disclosing to the prospective Human Subject information needed to make an informed decision; (2) facilitating the
understanding of what has been disclosed; and (3) promoting the voluntariness of the decision about whether or not to participate in the Research.

Informed consent is more than just a signature on a form. It is a process of information exchange to include reading and signing the informed consent document. The informed consent process is the critical communication link between the prospective Human Subject and an Investigator, beginning with the initial approach of an Investigator and continuing through the completion of the Research study. Investigators must have received the appropriate training and be knowledgeable about the study Protocol in order that they may answer questions to help provide understanding to the study Participant or potential study Participant. The exchange of information between the Investigator and study Participant can occur via one or more of the following modes of communication, among others; face to face contact, mail; telephone; or fax however obtaining informed consent must be obtained face to face between the Investigator and the potential study Participant/study Participant.

5.4 Informed Consent Process

Informed consent must be obtained under the following circumstances:

1. Informed consent may only be obtained from subjects who have the legal and mental capacity to give consent. For subjects without that capacity, consent must be obtained from a Legally Authorized Representative. See Section 6.10 for details regarding additional requirements for individuals with impaired decision making.

2. The informed consent process shall be sought under circumstances that provide the subject (or Legally Authorized Representative) with sufficient opportunity to consider whether or not to participate.

3. The informed consent process shall be sought under circumstances that minimize the possibility of coercion or undue influence. Coercion occurs when an overt or implicit threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast often occurs through an offer of an excessive or inappropriate reward or overture in order to obtain compliance.

4. The informed consent information must be presented in language that is understandable to the subject (or Legally Authorized Representative). To the extent possible, the language should be understandable by a person who is educated to 8th grade level and layman’s terms shall be used in the description of the Research.

5. For subjects whose native language is not English, informed consent must be obtained in a language that is understandable to the subject (or Legally Authorized Representative). In accordance with this policy, the IRB requires that informed consent conferences include a qualified translator when the prospective subject does not understand the language of the person who is obtaining consent. The Translator must sign the approved translated consent form as the witness.

6. The informed consent process may not include any exculpatory language through which the subject is made to waive, or appear to waive any of the subject’s legal rights or through which the Investigator, the Sponsor, the Institution or Tulane employees or Institutional Agents are released from liability for negligence, or appear to be so released. [DHHS 45 CFR §46.116; FDA 21 CFR §50.20].
7. The PI is ultimately responsible for ensuring that each prospective subject is adequately informed about all aspects of the Research and understands the information provided. However, the HRPO, the Research Investigators and the Research staff all share in the responsibility of ensuring that the informed consent process is adequate.

8. Federal regulations do not specify how far in advance of study entry a subject can provide consent. The amount of time required by a subject to make a decision would presumably depend upon the nature of the study, taking into consideration the degree of risk, potential benefits, alternatives, and desire to consult with family. For the sake of clarification, consents are current for 30 days but it may be prudent to review information contained in the consent document with the Research subject prior to initiating any Research procedures.


5.5 Basic Elements of Informed Consent

To be valid, the consent process must provide the following basic elements of information to potential subjects:

1. A statement that the study involves Research, an explanation of the purposes of the Research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental and done for Research purposes; a description of any reasonably foreseeable risks or discomforts to the subject including privacy risks (legal, employment, etc);

2. A description of any benefits to the subject or to others which may reasonably be expected from the Research;

3. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

4. A statement describing the extent, if any, to which confidentiality of records identifying the subject must be maintained;

5. For Research involving more than Minimal Risk, an explanation as to the availability of medical treatment in the case of Research-related injury, including who will pay for the treatment and whether other financial compensation is available;

6. An explanation of whom to contact on the Research team for answers to pertinent questions about the Research or to voice concerns or complaints about the Research, and whom to contact in the event of a Research-related injury to the subject;

7. Contact information for the IRB to obtain answers to questions about the Research; to voice concerns or complaints about the Research; to obtain answers to questions about their rights as a Research Participant; in the event the Research staff could not be reached; and in the event the subject wishes to talk to someone other than the Research staff.

8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may
discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled;

9. For FDA-regulated studies, the possibility that the FDA may inspect the records needs to be included in the statement regarding subject Confidentiality.

Regulations & Guidance: DHHS 45 CFR §46.116(a); FDA 21 CFR §50.25(a); OHRP Guidance on Exculpatory Language in Informed Consents; FDA Information Sheets: A Guide to Informed Consents; AAHRPP II.7.A.

5.6 Additional Elements of Informed Consent to be Applied, as Appropriate:

Additional situational-specific elements that an informed consent should include are:

1. A statement that the particular treatment or procedure may involve risks to the subject, which are currently unforeseeable. (e.g., include when the Research involves investigational Test Articles or other procedures in which the risks to subjects are not well known);

2. A statement that if the subject is or becomes Pregnant, the particular treatment or procedure may involve risks to the embryo or Fetus, which are currently unforeseeable (e.g., include when the Research involves Pregnant Women or women of childbearing potential and the risk to Fetuses of the Drugs, Devices, or other procedures involved in the Research is not well known);

3. Anticipated circumstances under which the subject’s participation may be Terminated by the Investigator without regard to the subject’s consent;

4. Any additional costs to the subject that may result from participation in the Research;

5. The consequences of a subject’s decision to withdraw from the Research (e.g., include when withdrawal from the Research is associated with adverse consequences);

6. Procedures for orderly termination of participation by the subject (e.g., include when the Protocol describes such procedures);

7. A statement that significant new findings developed during the course of the Research which may relate to the subject’s willingness to continue participation will be provided to the subject (e.g., include when the Research is long term and interim information is likely to be developed during the conduct of the Research);

8. The approximate number of subjects involved in the study (e.g., include when the Research involves more than Minimal Risk); and

9. Investigational New Drug Application (IND) submitted to FDA are not required to contain a copy of the consent document. For SR Devices, the consent document is considered to be a part of the investigational plan in the Application for an Investigational Device Exemption (IDE). Any Substantive changes to the document made by an IRB must be submitted to the FDA (by the Sponsor) for review and approval.

10. Use of a written translation of the entire IRB-approved English consent form is required for subjects who do not speak English and where researchers can reasonably expect that more than an incidental number of subjects speaking the same non-English language will be enrolled (e.g., if the Investigator is targeting a non-English speaking group). The IRB
must approve all translated versions of the consent form and recommends that the translation be done by a certified translator. However, the IRB will consider, on a case-by-case basis, allowing other translators to perform this function with verification that the translation is an accurate and acceptable presentation of the entire English version.

11. Investigators cannot always anticipate the interest of a particular non-English speaking individual and provide him/her with a translation of the entire IRB-approved English version of the informed consent document in a timely manner. Under these circumstances, a translation of the IRB-approved "short form" (which attests that the elements of consent have been presented orally) can be used to document informed consent in writing. **Short Form Consent Template** (TU Form 407). When a "short form" is used to document informed consent, the consent process must include oral presentation of the entire English version of the consent form in language understandable to the potential subject. See section 5.7.1 below for details with respect to necessary elements for a valid short form. The IRB recommends that an experienced translator be used. For questions about obtaining translations or whether a translator is sufficiently experienced contact HRPO.

Regulations & Guidance:  DHHS 45 CFR §46.116(b); FDA 21 CFR §50.25(b).

### 5.7 Documentation of Informed Consent

Except as provided in Section 5.9, informed consent must be documented by the use of a written consent form approved by the IRB and signed, dated and timed by the subject or the subject's Legally Authorized Representative at the time of consent. This includes non-therapeutic clinical trials (i.e., a trial in which there is no anticipated direct clinical benefit to the subject) should be conducted in subjects who personally give consent and who sign and date the written consent document. A copy of the signed and dated consent form must be given to the person signing the form.

The informed consent process must also be conducted and consent obtained in person in addition to reading and signing the informed consent document. Tulane does not allow for obtaining informed consent over the phone or by mail to ensure subject understanding and to allow for question/answer sessions. In addition to signing the consent document, the subject or representative should enter the date and time of signature on the consent document to permit verification that consent was actually obtained before the subject began participation in the study. If the consent is obtained on the same day as the subject’s involvement in the study begins, the subject’s medical records/source documentation should document that consent was obtained prior to participation in the study. A copy of the consent document should be provided to the subject, a copy placed on all of the appropriate Tulane medical records, and the original signed consent document should be retained in the study records. It is not required that the subject’s copy be a signed copy, although a photocopy with a signature is strongly preferred.

#### 5.7.1 Short Form Consent Documentation

For the short form of consent documentation, the IRB determines that the regulatory criteria for use of the short form of consent documentation are met.

1. The consent document states that the elements of disclosure required by regulations have been presented orally to the subject or the subject’s Legally Authorized Representative.
2. A written summary embodies the basic and appropriate additional elements of disclosure.
3. There will be a witness to the oral presentation.
4. For subjects who do not speak English, the witness will be conversant in both English and the language of the subject.
5. The subject or the subject’s Legally Authorized Representative will sign the consent document.
6. If the research is FDA-regulated, the subject or the subject’s Legally Authorized Representative will sign and date the consent document.
7. The witness will sign both the short form and a copy of the summary.
8. The person actually obtaining consent will sign a copy of the summary.
9. A copy of the short form will be given to the subject or the subject’s Legally Authorized Representative.
10. A copy of the summary will be given to the subject or the subject’s Legally Authorized Representative.
11. Copy of the IRB-approved Consents (TU Forms 402, 403, or 407).

5.7.2 Informed Consent-- Document Stamp Date
If the informed consent is to be documented, then the PI will receive, along with the approval letter, one copy of the IRB-approved consent form for the study that will have been stamped with the IRB approval date and expiration date. The PI is to make copies of the informed consent document that bears the IRB-approval stamp and use those copies for consenting study Participants.

Regulations & Guidance: DHHS 45 CFR §46.109(c); 45 CFR §46.117; FDA 21 CFR §50.27; AAHRPP II.7.D.

5.8 Consent Monitoring
In reviewing the adequacy of informed consent procedures for proposed Research, the IRB may on occasion determine that special monitoring of the consent process by an impartial observer (consent monitor) is required in order to reduce the possibility of coercion and undue influence, ensure that the approved consent process is being followed, or ensure that subjects are truly giving informed consent.

Such monitoring may be particularly warranted for:

- High risk studies;
- Studies that involve particularly complicated procedures or interventions;
- Studies involving highly Vulnerable Populations (e.g., ICU patients, Children);
- Studies involving study staff with Minimal Risk experience in administering consent to potential study Participants, or
- Other situations when the IRB has concerns that consent process is not being conducted appropriately.
Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with a particular Investigator or a Research project.

If the IRB determines that consent monitoring is required, the IRB Chair and the HRPO Director will develop a monitoring plan and submit it to the IRB for approval. The consent monitoring may be conducted by IRB staff, IRB members or another party, either affiliated or not with the Institution. The PI will be notified of the IRB(s) determination and the reasons for the determination. Arrangements will be made with the PI for the monitoring of the consent process for a specified number of subjects. When observing the consent process, the monitor will determine:

- Whether the informed consent process was appropriately completed and documented;
- Whether the Participant had sufficient time to consider study participation;
- Whether the consent process involved coercion or undue influence;
- Whether the information was accurate and conveyed in understandable language; and
- Whether the subject appeared to understand the information and gave their voluntary consent.

Following the monitoring, a report of the findings will be submitted to the IRB, which will determine the appropriate action to be taken.

5.9 Waiver of Informed Consent

An IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth above; or waive the requirements to obtain informed consent, provided the IRB finds and documents that:

- The Research involves no more than Minimal Risk tangible or intangible risk to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The Research could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the subjects must be provided with additional pertinent information after participation.

In addition, an IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent; or waive the requirements to obtain informed consent, provided the IRB finds and documents that:

- The Research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
  - Public benefit or service programs;
  - Procedures for obtaining benefits or services under those programs;
  - Possible changes in or alternatives to those programs or procedures; or
  - Possible changes in methods or levels of payment for benefits or services under those programs.
The Research could not practicably be carried out without the waiver or alteration. FDA regulations do not provide for waivers of informed consent except in emergency situations (See Section 7.4.3 and 7.5.6).

Regulations & Guidance: DHHS 45 CFR §46.116(c)-(d); FDA 21 CFR §50.23; AAHRPP II.7.E; II.7.F.

5.10 Waiver of Documentation of Informed Consent

The IRB may waive the requirement for the PI to obtain a signed consent form for some or all subjects if it finds either that the:

- Only record linking the subject and the Research would be the consent document and the principle risk would be potential harm resulting from a breach of Confidentiality;\(^\text{10,11}\) or
- The Research presents no more than Minimal Risk of harm to subjects and involves no procedures for which written consent is normally required outside of the Research context. Procedures such as non-sensitive surveys, questionnaires and interviews generally do not require written consent when conducted by non-Researchers.

In cases in which the documentation requirement is waived, the IRB requires the PI to provide in the application materials a written summary of the information to be communicated to the subject, and the IRB will consider whether to require the Investigator to provide subjects with a written statement regarding the Research.

The IRB Chair or primary reviewer will complete the checklist entitled “Supplement - Waiver of Requirements for Documentation of Informed Consent” contained in the IRB Application (TU Form 102). In addition, the IRB minutes will document required determination regarding waiver of requirements for written documentation of informed consent. The minutes also will document the Protocol specific findings justifying the requirements.

Regulations & Guidance: DHHS 45 CFR §46.109(c); 45 CFR §46.117; AAHRPP II.7.E.

---

\(^{10}\) Subjects must be asked whether they want documentation linking them with the Research, and their wishes must govern. (Example: domestic violence Research where the primary risk is discovery by the abuser that the subject is talking to Researchers.)

\(^{11}\) In order to waive written documentation of consent where the only record linking the Participant and the Research would be the consent document, the IRB has to determine that the Research was not FDA-regulated.
6 Vulnerable Subjects in Research

6.1 Policy

When some or all of the Participants in a Research Under the Auspices of the Institution’s IRB are likely to be vulnerable to coercion or undue influence or have diminished decision-making capacity, the Research must include additional safeguards to protect the rights and welfare of these Participants. The IRB must ensure that all of the regulatory requirements for the protection of Vulnerable Subjects are met and that appropriate additional protections for Vulnerable Subjects are in place.

The following procedures describe the requirements for involving vulnerable Participants in Research Under the Auspices of the Institution’s IRB.

6.2 Involvement of Vulnerable Populations

When some or all of the Participants in a Protocol are likely to be vulnerable to coercion or undue influence, the IRB should include additional safeguards to protect the rights and welfare of these Participants. Some of the Vulnerable Populations that might be involved in Research include individuals who are educationally or financially disadvantaged, Children, Pregnant Women, Fetuses, Neonates, Prisoners, or economically or educationally disadvantaged, or adults who lack the ability to consent, students, employees, or homeless persons.

If the IRB reviews Research that involves categories of Participants vulnerable to coercion or undue influence, the review process will include one or more individuals who are knowledgeable about or experienced in working with these Participants. For example, the IRB will include one or more individuals who are knowledgeable about or experienced in working with Children, Prisoners, or adults with limited decision-making capacity, when reviewing Research that involves individuals from these populations.

Additional requirements for IRB oversight of Research involving Vulnerable Populations can be found at 45 CFR § part 46, which includes the following:

- Subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research;
- Subpart C - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects; and
- Subpart D - Additional Protections for Children Involved as Subjects in Research.

DHHS-funded research that involves any of these populations must comply with the requirements of the relevant subparts. Research funded by other federal agencies may or may not be covered by the subparts.

Under Tulane’s FWA the subparts only apply to DHHS-funded research and research funded by another federal agency that requires compliance with the subparts (FDA regulations include Subpart D, which applies to all FDA-regulated research). The following policies and procedures, which are based on the subparts, apply to all research regardless of funding. The individual sections describe how the subparts apply to DHHS-funded research.
6.3 Definitions

_Vulnerable Population (or “Vulnerable Subjects”):_ This includes the following classes of potential or actual Research subjects: Children, Prisoners, Pregnant Women, mentally-disabled persons, or economically- or educationally-disadvantaged persons.

6.4 Responsibilities

1. The PI is responsible for identifying the potential for enrolling Vulnerable Subjects in the Research Proposal. The PI is responsible for identifying patients who are at risk for impaired decisional capacity as a consequence of psychiatric illness, and who are being asked to participate in a Research study with greater than Minimal Risk.

2. The IRB shall include representation, either as members or ad hoc consultants, individual(s) interested in or who have experience with the Vulnerable Populations involved in a Research Proposal.

3. The IRB reviews the PI’s justifications for including Vulnerable Populations in the Research to assess appropriateness of the Research Proposal.

4. The IRB must ensure that additional safeguards have been included in each study to protect the rights and welfare of Vulnerable Subjects as needed at the time of Initial Review of the Research Proposal.

5. The IRB shall continue to review Research at intervals appropriate to the degree of risk and determine whether the proposed Research continues to fulfill criteria for approval. Information reviewed should include the number of Participants considered as members of specific Vulnerable Populations.

6. For studies that do not have or are not required to have a DSMB or a Data Monitoring Committee and have entered Vulnerable Subjects, the IRB needs to carefully review the DSM plan.

7. The IRB should be knowledgeable about and experienced in working with populations who are vulnerable to coercion and undue influence. If the IRB requires additional qualification or expertise to review a Protocol, it should obtain consultation.

6.5 Procedures

6.5.1 Initial Review of Research Proposal:

The following steps are relevant with respect to initial review of a Research Proposal:

1. The PI should identify the potential to enroll Vulnerable Subjects in the proposed Research at Initial Review and provide the justification for their inclusion in the study.

2. The IRB evaluates the proposed plan for consent of the specific Vulnerable Populations involved. If the Research involves adults unable to consent, the IRB evaluates the proposed plan for permission of Legally Authorized Representatives.

3. The IRB evaluates and approves the proposed plan for the Assent of Participants.

4. The IRB evaluates the Research to determine the need for additional protections and consider the use of a DSMB or data safety monitoring committee, as appropriate.
5. The PI should provide appropriate safeguards to protect the subject’s rights and welfare, which may include the addition of an independent monitor. The independent monitor is a qualified individual not involved in the Research study who will determine the subject’s capacity to provide voluntary informed consent. Populations requiring independent monitoring might include individuals with schizophrenia, other psychotic disorders or conditions characterized by lack of reality testing (i.e., psychosis). Populations not usually requiring independent monitoring would include those with substance use disorders.

6. The IRB assess the adequacy of additional protections for Vulnerable Populations provided by the PI.

6.5.2 Continuing Review and Monitoring.
At Continuing Review, the PI should identify the number of Vulnerable Subjects enrolled and any that needed an independent monitor in the progress report.

6.6 Research Involving Pregnant Women or Fetuses

6.6.1 Definitions
Dead Fetus: is a Fetus that exhibits neither a heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord, if still attached. [DHHS 45 CFR 46§202(a)].

Delivery: means complete separation of the Fetus from the woman by expulsion, extraction, or any other means.

Fetus: is the product of conception (i.e., fusion of a human spermatozoa with a human ova) from the time of implantation until Delivery. [DHHS 45 CFR §46.202(c); LA R.S. 40:1299.35.1].

Pregnant (or Pregnancy): is the period of time from confirmation of implantation (through any of the presumptive signs of pregnancy, such as missed menses, or by a medically acceptable pregnancy test), until expulsion or extraction of the Fetus. [DHHS 45 CFR §46.202(f)].

6.6.2 Research Not Funded by DHHS
For Research not funded by DHHS, no additional safeguards are required by the regulations and there are no restrictions on the involvement of Pregnant Women in Research where the risk to the Fetus is no more than Minimal Risk.

Pregnant Women or Fetuses may be involved in Research not funded by DHHS involving more than Minimal Risk to Fetuses if all of the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-Pregnant Women, have been conducted and provide data for assessing potential risks to Pregnant Women and Fetuses;
2. The risk to the Fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the Fetus;
3. Any risk is the least possible for achieving the objects of the Research;
4. If the Research holds out the prospect of direct benefit to the Pregnant woman, the prospect of a direct benefit both to the Pregnant woman and the Fetus, then the consent
of the Pregnant woman is obtained in accordance with the provisions for informed consent;

5. If the Research holds out the prospect of direct benefit solely to the Fetus then the consent of the Pregnant woman and the father is obtained in accordance with the provisions for informed consent, except that the father’s consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the Pregnancy resulted from rape or incest;

6. Each individual providing consent under paragraph 4 or 5 of this Section is fully informed regarding the reasonably foreseeable impact of the Research on the Fetus or Neonate;

7. For Children who are Pregnant, Assent and permission are obtained in accordance with the provisions of permission and Assent (see Section 6.9.3.3);

8. No inducements, monetary or otherwise, will be offered to terminate a Pregnancy;

9. Individuals engaged in the Research will have no part in any decisions as to the timing, method, or procedures used to terminate a Pregnancy; and

10. Individuals engaged in the Research will have no part in determining the viability of a Neonate.

Regulations & Guidance: DHHS 45 CFR § 46.204.

6.6.3 Research Funded by DHHS

For DHHS-funded Research, 45 CFR Subpart B applies to all Research involving Pregnant Women. According to 45 CFR Subpart B, Pregnant Women or Fetuses may be involved in Research funded by DHHS if all of the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-Pregnant Women, have been conducted and provide data for assessing potential risk to Pregnant Women and Fetuses.

2. The risk to the Fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the Fetus or, if there is no such prospect of benefit, the risk to the Fetus is not greater than Minimal Risk and the purpose of the Research is the development of important biomedical knowledge which cannot be obtained by any other means;

3. Any risk is the least possible for achieving the objects of the Research;

4. If the Research holds out the prospect of direct benefit to the Pregnant woman, the prospect of a direct benefit both to the Pregnant woman and the Fetus, or no prospect of benefit for the woman nor the Fetus when risk to the Fetus is not greater than Minimal Risk and the purpose of the Research is the development of important biomedical knowledge that cannot be obtained by any other means, then the consent of the Pregnant woman is obtained in accordance with the provisions for informed consent.

5. If the Research holds out the prospect of direct benefit solely to the Fetus then the consent of the Pregnant woman and the father is obtained in accordance with the provisions for informed consent, except that the father’s consent need not be obtained if he is unable to
consent because of unavailability, incompetence, or temporary incapacity or the Pregnancy resulted from rape or incest.

6. Each individual providing consent under paragraph 4 or 5 of this Section is fully informed regarding the reasonably foreseeable impact of the Research on the Fetus or Neonate;

7. For Children who are Pregnant, Assent and permission are obtained in accord with the provisions of permission and Assent in Section 6.9.3.3;

8. No inducements, monetary or otherwise, will be offered to terminate a Pregnancy;

9. Individuals engaged in the Research will have no part in any decisions as to the timing, method, or procedures used to terminate a Pregnancy; and

10. Individuals engaged in the Research will have no part in determining the viability of a Neonate.

6.7 Research Involving Neonates

6.7.1 Definitions

**Neonate**: means Newborn. [DHHS 45 CFR 46.202(d)].

**Neglect**: Neglect of Neonate means a medical finding by a Louisiana licensed physician that a Neonate either is dependent upon or suffers from withdrawal symptoms from an illegal controlled dangerous substance (“CDS”). It also includes a medical finding by a physician that a Neonate suffers from an illness, disease or condition attributable to the exposure of the newborn, in utero, of an illegal CDS.

**Non-Viable Neonate (or “Non-Viable Fetus”)**: is a Fetus ex utero that, although living, is not able to survive to the point of independently maintaining a heartbeat and respiration. [DHHS CFR 46.202(e)].

**Viable Neonate (or “Viable Fetus”)**: Means a Fetus that is able, after Delivery, to survive to the point of being able to independently maintain a heartbeat and respiration (given the benefit of available medical therapy). [DHHS 45 CFR §102(c) & (l); 45 CFR §46.202(h)].

6.7.2 General Requirement Regarding Research Involving Neonates

Neonates of uncertain viability and Non-Viable Neonates may be involved in Research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to Neonates;

2. Each individual that’s providing consent is fully informed regarding the reasonably foreseeable impact of the Research on the Neonate; and

3. Individuals engaged in the Research will have no part in determining the viability of a Neonate.

The requirements of Neonates of Uncertain Viability or Non-Viable Neonates (see below in this Section) have been met as applicable.

Regulations & Guidance: DHHS 45 CFR §46.205(a).
6.7.3 Neonates of Uncertain Viability.

Until it has been ascertained whether or not a Neonate is viable, a Neonate may not be involved in Research covered by this subpart unless the following additional conditions have been met:

The IRB determines that:

1. The Research holds out the prospect of enhancing the probability of survival of the Neonate to the point of viability, and any risk is the least possible for achieving that objective; or

2. The purpose of the Research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the Neonate resulting from the Research; and

3. The legally effective informed consent of either Parent of the Neonate or, if neither Parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either Parent’s Legally Authorized Representative is obtained in accordance with the provisions of permission and Assent, except that the consent of the father or his Legally Authorized Representative need not be obtained if the Pregnancy resulted from rape or incest.

Regulations & Guidance: DHHS 45 CFR §46.205(b).

6.7.4 Non-Viable Neonates.

After Delivery, Non-Viable Neonates may not be involved in Research covered by this subpart unless all of the following additional conditions are met:

1. Vital functions of the Neonate will not be artificially maintained;

2. The Research will not terminate the heartbeat or respiration of the Neonate;

3. There will be no added risk to the Neonate resulting from the Research;

4. The purpose of the Research is the development of important biomedical knowledge that cannot be obtained by other means; and

5. The legally effective informed consent of both Parents of the Neonate is obtained in accordance with the provisions of permission and Assent, except that the waiver and alteration of the provisions of permission and Assent do not apply.

6. However, if either Parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one Parent of a Non-Viable Neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the Pregnancy resulted from rape or incest. The consent of a Legally Authorized Representative of either or both of the Parents of a Non-Viable Neonate will not suffice to meet the requirements of this paragraph.

Regulations & Guidance: DHHS 45 CFR §46.205(c).

6.7.5 Viable Neonates.

A Neonate, after Delivery, that has been determined to be viable may be included in Research only to the extent permitted by and in accordance with the requirements of IRB Review Process and Research Involving Children. [DHHS 45 CFR §46.205(d)].
6.7.6  Research involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material

Research involving, after Delivery, the placenta; the dead Fetus; macerated fetal material; or cells, tissue, or organs excised from a dead Fetus, must be conducted only in accordance with any applicable Federal, State, or local laws and regulations regarding such activities.

If information associated with material described above in this Section is recorded for Research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are Research subjects and all pertinent Sections of this document are applicable. [DHHS 45 CFR §46.206].

6.7.7  Research Not Otherwise Approvable

6.7.7.1  Research Not Funded by DHHS

If the IRB finds that the Research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of Pregnant Women, Fetuses or Neonates; and the Research is not approvable under the above provisions, then the IRB will consult with a panel of experts in pertinent disciplines (e.g., science, medicine, ethics, and law). Based on the recommendation of the panel, the IRB may approve the Research based on either:

1. That the Research in fact satisfies the conditions of Section 6.6, as applicable; or

2. The following:
   a. The Research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of Pregnant Women, Fetuses or Neonates;
   b. The Research will be conducted in accordance with sound ethical principles; and
   c. Informed consent will be obtained in accordance with the provisions for informed consent and other applicable Sections of this document.

Regulations & Guidance: DHHS 45 CFR §46.207.

6.7.7.2  Research Funded by DHHS

DHHS-funded Research that falls in this category must be approved by the Secretary of DHHS. If the IRB finds that the Research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of Pregnant Women, Fetuses or Neonates; and the Research is not approvable under the above provisions, then the Research will be sent to OHRP for DHHS review.

6.8  Research Involving Prisoners

Research conducted under the auspices of Tulane’s IRB is subject to the following requirements.

Prisoners are another class deemed so vulnerable to exploitation in Research that there are special rules protecting them. In the past, Prisoners were viewed as a convenient Research population because they are housed in a single location, constitute a large and relatively stable population, and live a routine life. Unfortunately, all the things that make a prison and Prisoners a convenient Research population also make Prisoners ripe for exploitation. The challenge is to ensure that Prisoners have a real choice when they decide whether to participate in Research.
6.8.1 Definitions

**Minimal Risk for Prisoners**: is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. [DHHS 45 CFR §46.102(i); 45 CFR §46.303(d); FDA 21 CFR §50.3(k); 21 CFR §56.102(i)]. The definition of Minimal Risk for Prisoners contained in the Subpart C of the Federal regulations is different than the definition of Minimal Risk (for non-Prisoners).

**Prisoner**: is any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing. [DHHS 45 CFR §46.303(c)].

6.8.2 Applicability

The requirements in this Section apply to all Research involving Prisoners under the purview of the Institution’s IRB, regardless of the funding source. Even though the IRB may approve a Research Protocol involving Prisoners as subjects according to this policy, Investigators also are still subject to the Administrative Regulations of the Louisiana Department of Corrections and any other applicable State or local law. [DHHS 45 CFR §46.301].

6.8.3 Composition of the IRB

In addition to satisfying the general requirements detailed in the IRB section of this document, when reviewing Research involving Prisoners, the IRB must also meet the following requirements:

- A majority of the IRB (exclusive of Prisoner members) must have no association with the prison(s) involved, apart from their membership on the IRB; and
- At least one member of the IRB must be a Prisoner, or a Prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular Research project is reviewed by more than one IRB, only one IRB need to satisfy this requirement.

Regulations & Guidance: DHHS 45 CFR §46.304.

6.8.4 Additional Duties of the IRB

In addition to all other IRB responsibilities prescribed in this document, the IRB will review Research involving Prisoners and approve such Research only if it finds that:

- The Research falls into one of the following permitted categories [45 CFR §46.306]:
  - Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than Minimal Risk for Prisoners and no more than inconvenience to the subjects;
  - Study of prisons as institutional structures or of Prisoners as incarcerated persons, provided that the study presents no more than Minimal Risk for Prisoners and no more than inconvenience to the subjects;
Research on conditions particularly affecting Prisoners as a class (e.g., research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults); and
Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject.

- Any possible advantages accruing to the Prisoner through this or her participation in the Research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the Research against the value of such advantages in the limited choice environment of the prison is impaired;
- The risks involved in the Research are commensurate with risks that would be accepted by non-Prisoner volunteers;
- Procedures for the selection of subjects within the prison are fair to all Prisoners and immune from arbitrary intervention by prison authorities or Prisoners. Unless the PI provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available Prisoners who meet the characteristics needed for that particular Research project;
- The information is presented in language which is understandable to the subject population;
- Adequate assurance exists that parole board will not take into account a Prisoner’s participation in the Research in making decisions regarding parole, and each Prisoner is clearly informed in advance that participation in the Research will have no effect on his or her parole; and
- Where the IRB finds there may be a need for follow-up examination or care of subjects after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual Prisoners’ sentences, and for informing subjects of this fact.

Regulations & Guidance: DHHS 45 CFR §46.305.

6.8.5 Waiver for Epidemiology Research involving Prisoners
The Secretary of DHHS has waived the applicability of 45 CFR §46.305(a)(l) and 46.306(a)(2) (see Section 6.8.4 for details) for certain Research conducted or supported by DHHS that involves epidemiologic studies that meet the following criteria:

1. In which the sole purposes are
   - To describe the prevalence or incidence of a disease by identifying all cases; or
   - To study potential risk factor associations for a disease; and
2. Where the IRB has approved the Research and fulfilled its duties under 45 CFR §46.305(a)(2)–(7) and determined and documented that:
   - The Research presents no more than Minimal Risk for Prisoners and no more than inconvenience to the Prisoner-subjects; and
   - Prisoners are not a particular focus of the Research; and
3. The specific type of epidemiological Research subject to the waiver involves no more than Minimal Risk for Prisoners and no more than inconvenience to the Human Subject Participants. The waiver would allow the conduct of Minimal Risk for Prisoners Research that does not now fall within the categories set out in 45 CFR §46.306(a) (2); and

4. The range of studies to which the waiver would apply includes epidemiological Research related to chronic diseases, injuries, and environmental health. This type of Research uses epidemiologic methods (such as interviews and collection of biologic specimens) that generally entail no more than Minimal Risk for Prisoners to the subjects; and

5. In order for a study to be approved under this waiver, the IRB would need to ensure that, among other things, there are adequate provisions to protect the Privacy of subjects and to maintain the Confidentiality of the data.

6.9 Research Involving Children

The following applies to all Research involving Children, regardless of funding source. The requirements in this Section are consistent with Subpart D of 45 CFR 46 (applicable to DHHS-funded Research) and Subpart D of 21 CFR 50 (applies to FDA-regulated Research involving Children).

Regulations & Guidance: FDA 21 CFR §56.109(h); 21 CFR §56.111(c)].

6.9.1 Definitions

**Assent:** means a Child’s affirmative agreement to participate in Research. Mere failure of a Child to object may not, absent affirmative agreement, be construed as Assent. [FDA 21 CFR §50.3(n)].

**Child (or “Children”):** are persons who have not attained the legal age for consent to treatments or procedures involved in the Research, under the applicable law of the jurisdiction in which the Research will be conducted. [DHHS 45 CFR §46.402(s); FDA 21 CFR §50.3(o)].

According to Louisiana Law, the legal age for consent for treatment or medical procedures is 18 years or older. [LA Children’s Code 116; LA R.S. 40:1095]. Louisiana law is silent with respect to the legal age to consent with respect to Research. For purposes of these SOPs, any person who is under the age of 18 generally is unable to consent for him/herself. Several important exceptions exist under Louisiana law that effectively treat Children as adults and gives them the capacity to consent to their own medical care and to participate in Research. They include the following:

- For a Child to receive medical and/or surgical care at a hospital and/or to receive physicians’ services [LA R.S. 40:1095]. This may or may not overlap with the proposed Research;
- If a Child is emancipated by marriage. Regardless of age, a Child is fully emancipated upon his or her marriage [LA Children’s Code Art 379];
- If a Child is judicially emancipated. This requires a court order for Child older than 16 years of age [LA Children’s Code Art 366 and 1922];
- If a Child is emancipated by authentic act. This requires a Child older than 16 years of age and the Child’s Parents to execute a written document of emancipation, signed before 2 witnesses and a notary [LA Children’s Code Art 368];

- If a Child seeks to be treated for venereal disease [LA R.S. 40:1065.1]; and

- If a Child seeks to be treated for drug abuse [LA R.S. 40:1096].

Because Louisiana law does not specifically address consent of Children with majority status to Research, the University’s IRB will review issues of consent related to enrollment of these Children in Research on a case-by-case basis.

Regulations & Guidance: AAHRPP I.3.F.

**Guardian (or Legal Guardian):** means an individual who is authorized under applicable State or local law to consent on behalf of a Child to (a) general medical care when general medical care includes participation in Research; or (b) to participate in Research. [DHHS 45 CFR §46.402(e); FDA 21 CFR 50.3(s); LA. Children’s Code 116(12.1)(a)(i)(b)]. A Guardian of a Minor retains the duty and authority to (1) act in the best interests of the Minor, subject to residual parental rights and responsibilities (if any); (2) make important decisions in matters having a permanent effect on the life and development of the Minor; and (3) to be concerned with the Minor’s general welfare. For Research conducted in jurisdictions other than Louisiana, the Research must comply with the laws regarding guardianship in all relevant jurisdictions where the Research will take place.

**Health Agent:** Is an authorized representative legally acting for a person pursuant to a Durable Power of Attorney for Health Care ("Medical Power of Attorney") or other legal document permitted within a jurisdiction that allows a person to appoint another person(s) to make medical decisions for the patient if the patient should become temporarily or permanently unable to make those decisions for himself/herself. Any adult (18 or older) can be granted this power. [LA R.S.40:1299.53(A)(13)].

**Legally Authorized Representative:** is an individual, judicial, or other body authorized under applicable law to consent or otherwise provide permission on behalf of a subject, either prospectively or during the course of Research, to the subject's participation in the procedure(s) involved in the Research. [DHHS 45 CFR §46.102(c); FDA 21 CFR §50.3(l)]. For the purposes of this document, a Legally Authorized Representative includes a person appointed as a Health Agent, a court-appointed Legal Guardian of the person, as well as next-of-kin in the following order of priority unless otherwise specified by applicable State law: the subject’s spouse; adult Child(ren) of subject (18 years of age or older); Parent of subject; adult sibling(s) of subject (18 years of age or older); grandparent(s) of subject; or adult grandchild(ren) of subject (18 years of age or older). If there is more than one person within the above named class, the consent shall be given by a majority of those members of the class available for consultation.[LA R.S. 40:1299.53] Legally Authorized Representative should not be confused with Legal Guardian.

**Minor** means any person under the age of 18 years. [LA Children’s Code Art 116]. Do not confuse the definitions of Minor (pertaining to a person’s age) with Child/Children (pertaining to a person’s ability to consent).

**Parent** means a Child’s biological or adoptive parent. [FDA 21 CFR §50.3(p)].
6.9.2 Allowable Categories

Research on Children must be reviewed and categorized by the IRB into one of the following groups:

1. **Not Greater Than Minimal Risk**: Research on Children not involving physical or emotional risk greater than that ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (i.e., Minimal Risk). This includes adequate provisions are made for soliciting the Assent of Children and the permission of their Parents or Legal Guardians as set forth in Section 6.9.3.

2. **Greater Than Minimal Risk**: Research on Children involving greater than Minimal Risk but presenting the prospect of direct benefit to the individual subject.
   - The risk is justified by the anticipated benefit to the subjects;
   - The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
   - Adequate provisions are made for soliciting the Assent of Children and the permission of their Parents or Legal Guardians as set forth in Section 6.9.3.

3. **Greater Than Minimal Risk & No Prospect of Direct Benefit**: Research on Children involving greater than Minimal Risk and no reasonable prospect of direct benefit to the individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.
   - The risk represents a minor increase over Minimal Risk;
   - The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
   - The intervention or procedure is likely to yield generalizable knowledge about the subjects’ disorder or condition which is of vital importance to the understanding of amelioration of the subjects’ disorder or condition; and
   - Adequate provisions are made for soliciting the Assent of Children and the permission of their Parents or Legal Guardians as set forth in Section 6.9.3.

4. **Research Not Otherwise Approvable**: Research on Children not otherwise approvable which presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of Children.
   - Federally-funded Research in this category must be approved by the DHHS Secretary, and requires consent of either both Parents or the Legal Guardian.
   - FDA-regulated Research in this category must be approved by the FDA Commissioner.
   - For non-Federally-funded Research, the IRB will consult with a panel of experts in pertinent disciplines (e.g., science, medicine, ethics, or law). Based on the recommendation of the panel, the IRB may approve the Research based on either:
That the Research in fact satisfies the conditions of the previous categories, as applicable; or

The following:

- The Research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of Children;
- The Research will be conducted in accordance with sound ethical principles; and
- Informed consent will be obtained in accordance with the provisions for informed consent and other applicable Sections of this document.

Adequate provisions are made for soliciting the Assent of Children and the permission of their Parents or Legal Guardians as set forth in Section 6.9.3.


6.9.3 Parental Permission and Assent

6.9.3.1 Parental Permission

Since a Child cannot consent for him/herself, the IRB must determine that adequate provisions have been made for soliciting the permission of each Child’s Parent or Legal Guardian, as documented in the Consent (TU Forms 402, 403).

Consent should be obtained as follows in this order of priority:

- Mother and father [LA Children’s Code Art 216, 217] or adoptive foster parents [LA Children’s Code Art 40:1299.55]. The right first rests with married Parents of the Child. If they consent, comply with their wishes (subject to the Assent requirements below). If they do not agree, the father’s choice prevails [LA Children’s Code Art 216].
- A power of attorney from the Child’s Parents to another adult [LA Children’s Code Art 216 and 951, et seq];
- The court recognized tutor/tutrix [LA Children’s Code Art 246 and 253]; or
- A power of attorney from the Child’s tutor/tutrix to another adult [LA R.S. 9:951].

For Research conducted in jurisdictions other than Louisiana, the Research must comply with the laws regarding the legal age of consent in all relevant jurisdictions. The University Associate General Counsel for Research will provide assistance to the HRPO and PIs with regard to the laws in other jurisdictions.

Parents or Legal Guardians must be provided with the basic elements of consent and any additional elements the IRB deems necessary, as described in Section 5.5.

In addition to the requirements under Louisiana law, the IRB may find that the permission of one Parent is sufficient for Research to be conducted under Categories 6.9.2.1 & 6.9.2.2 above. Consent from both Parents is required for Research to be conducted under Categories 6.9.2.3 & 6.9.2.4 above unless:
1. One Parent is deceased, unknown, incompetent, or not reasonably available; or
2. When only one Parent has legal responsibility for the care and custody of the Child.

For Research not covered by the FDA regulation, the IRB may waive the requirement for obtaining consent from a Parent or Legal Guardian if:

- The Research meets the provisions for waiver in Section 5.8 or
- If the IRB determines that the Research Protocol is designed for conditions or a subject population for which Parental or Legal Guardian permission is not a reasonable requirement to protect the subjects (e.g., neglected or abused Children) provided an appropriate mechanism for protecting the Children who will participate as subjects in the Research is substituted, and that the waiver is not inconsistent with Federal, State, or local laws. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the Protocol, the risk and anticipated benefit to the Research subjects, and their age, maturity, status, and condition.

Parental permission may not be waived for Research covered by the FDA regulations.

Permission from Parents or Legal Guardians must be documented in accordance with and to the extent required by Sections 5.7 and 5.10.

Regulations & Guidance: DHHS 45 CFR §46.408; AAHRPP I.3.F.

6.9.3.2 Assent from Children

Because “assent” means a Child’s affirmative agreement to participate in Research, the Child must actively show his or her willingness to participate in the Research, rather than just complying with directions to participate and not resisting in any way. When judging whether Children are capable of Assent, the IRB is charged with taking into account the ages, maturity, and psychological state of the Children involved.

The IRB should take into account the nature of the proposed Research activity and the ages, maturity, and psychological state of the Children involved when reviewing the proposed Assent procedure and the form and content of the information conveyed to the prospective subjects. For Research activities involving adolescents whose capacity to understand resembles that of adults, the Assent procedure should likewise include information similar to what would be provided for informed consent by adults or for Parental permission. For Children whose age and maturity level limits their ability to fully comprehend the nature of the Research activity but who are still capable of being consulted about participation in Research, it may be appropriate to focus on conveying an accurate picture of what the actual experience of participation in Research is likely to be (e.g., what the experience will be, how long it will take, whether it might involve any pain or discomfort). The Assent procedure should reflect a reasonable effort to enable the Child to understand, to the degree they are capable, what their participation in Research would involve.

The IRB presumes that Children ages 7 and older should be given an opportunity to provide Assent. Generally, oral Assent through the use of a script should be obtained from Children 7 - 11 years of age. Written Assent using a written document for the Children to sign may be sought for older Children.

At times there may be inconsistency between Parent permission and Child Assent. Usually a "no" from the Child overrides a "yes" from a Parent, but a Child typically cannot decide to be in
Research over the objections of a Parent. Obviously, there are individual exceptions to these guidelines (such as when the use of an experimental treatment for a life threatening disease is being considered). The general idea, however, is that Children should not be forced to be Research subjects, even when their Parents consent to it.

If the IRB determines that the capability of some or all of the Children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the Research holds out a prospect of direct benefit that is important to the health or well-being of the Children and is available only in the context of the Research, the Assent of the Children is not a necessary condition for proceeding with the Research.

Even when the IRB determines that the subjects are capable of Assenting, the IRB may still waive the Assent requirement under circumstances detailed in the Waiver of Informed Consent Section of this document.

Regulations & Guidance: DHHS 45 CFR §46.408.

6.9.3.3 Consent from Pregnant Minors

A Minor may consent to medical care or the administration of medication by a hospital licensed to provide hospital services or by a physician licensed to practice medicine for the purpose of alleviating or reducing pain, discomfort, or distress of and during labor and childbirth. [LA R.S. 40:1095(A)(2)]. This consent shall be valid and binding as if the Minor had achieved her majority, and it shall not be subject to a later disaffirmance by reason of her Minority.

If Research pertains to such permitted Minor consent, then the Minor may consent to the involved Research. If not and the IRB has not waived the consent requirement, then Assent from the Minor is required, as well as Parental permission.

6.9.4 Assent Form

When the IRB determines that Assent is required, it shall also determine whether and how Assent must be documented.

Researchers should try to draft a form that is age appropriate and study specific, taking into account the typical Child's experience and level of understanding, and composing a document that treats the Child respectfully and conveys the essential information about the study. The Assent Form (TU Form 401) should:

1. Tell why the Research is being conducted;
2. Describe what will happen and for how long or how often;
3. Say it's up to the Child to participate and that it is permissible to say no;
4. Explain if it will hurt and if so for how long and how often;
5. Say what the Child's other choices are;
6. Describe any good things that might happen;
7. Say whether there is any compensation for participating; and
8. Ask for questions.
For younger Children, the document should be limited to one page if possible. Illustrations might be helpful, and larger type makes a form easier for young Children to read. Studies involving older Children or adolescents should include more information and may use more complex language.

6.9.5 Children who are Wards of the State

Children who are wards of the State or any other agency, institution, or entity can be included in Research involving greater than Minimal Risk where there is no prospect of direct benefits to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition, only if such Research is:

1. Related to their status as wards; or
2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of Children involved as subjects are not wards.

If the Research meets the condition(s) above, an advocate must be appointed by the IRB or Institution for each Child who is a ward (one individual may serve as advocate for more than one Child), in addition to any other individual acting on behalf of the Child as Legal Guardian or in loco parentis.

The advocate must be an individual who has the background and experience to act in, and agrees to act in, the best interests of the Child for the duration of the Child's participation in the Research and who is not associated in any way (except in the role as advocate or member of the IRB) with the Research, the Investigator(s), or the guardian organization.

Regulations & Guidance: DHHS 45 CFR §46.409.

6.10 Persons with Impaired Decision Making Capacity

The requirements in this Section apply to all Research involving persons with mental disabilities or persons with impaired decision-making capacity regardless of funding source.

Research involving persons with impaired decision-making capability may only be approved when the following conditions apply:

1. Only incompetent persons or persons with impaired decision making capacity (as determined by licensed health care professionals who are qualified to make such determinations consistent with the scope of their license) are suitable as Research subjects. Competent persons are not suitable for the proposed Research. The PI must demonstrate to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as subjects. Incompetent persons or persons with impaired decision-making capacity must not be subjects in Research simply because they are readily available.

2. The proposed Research entails no significant risks, tangible or intangible, or if the Research presents some probability of harm, there must be at least a greater probability of direct benefit to the Participant. Incompetent people or persons with impaired decision-making capacity are not to be subjects of Research that imposes a risk of injury, unless that Research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.
3. Procedures have been devised to ensure that Participant’s representatives are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision making capacity. Health Agents (appointed under Medical Power of Attorney) and next-of-kin, or Legal Guardians, must be given descriptions of both proposed Research studies and the obligations of the person’s representatives. They must be told that their obligation is to try to determine what the subject would do if competent, or if the subject's wishes cannot be determined, what they think is in the incompetent person's best interest. In addition and as appropriate, if Assent can be obtained by a subject/potential subject with diminished decision making capacity (versus impaired), then the PI should obtain such Assent. The determination as to whether an individual retains capacity to Assent must be determined by a duly qualified health care provider, consistent with the provider’s scope of licensure.

4. A non-therapeutic clinical trial (i.e., a trial in which there is no anticipated direct clinical benefit to the subject) should be conducted in subjects who personally give consent and who sign and date the written consent document. Non-therapeutic clinical trials may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled:
   a. The objectives of the trial cannot be met by means of a trial in subjects who can give consent personally;
   b. The foreseeable risks to the subjects are low.
   c. The negative impact on the subject’s well-being is minimized and low.
   d. The trial is not prohibited by law.
   e. The opinion of the IRB is expressly sought on the inclusion of such subjects, and the written opinion covers this aspect.
   f. Unless an exception is justified, the trial should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in such trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

Regulations & Guidance: AAHRPP II.7.B.

6.10.1 IRB composition

The IRB membership must include at least one member who is an expert in the area of the Research. Consideration may be given to adding another member who is a member of the population, a family member of such a person or a representative of an advocacy group for that population. The IRB may utilize ad hoc members as necessary to ensure appropriate scientific expertise.

6.10.2 Determination of Decision-Making Capacity

The decision-making capacity of a potential Research subject should be evaluated when there are reasons to believe that the subject may not be capable of making voluntary and informed decisions about Research participation.
The PI and Research staff must have adequate procedures in place for assessing and ensuring subjects’ capacity, understanding, and informed consent or Assent. The IRB will evaluate whether the proposed plan to assess capacity to consent is adequate.

For Research Protocols that involve subjects with mental disorders that may affect decision-making capacity, the IRB may determine that capacity assessments are necessary, unless the PI can justify why such assessments would be unnecessary for a particular group.

For Research that poses greater than Minimal Risk, the IRB may require Investigators to use independent and qualified professionals to assess whether potential subjects have the capacity to give voluntary, informed consent. Even in Research involving only Minimal Risk, the IRB may require that the study include a capacity assessment if there are reasons to believe that potential subjects’ capacity may be impaired. It is not necessary to require a formal capacity assessment by an independent professional for all potential Research subjects with mental disorders. See the next Section for details with respect to determining capacity to consent.

For Research Protocols involving subjects who have fluctuating or limited decision making capacity the IRB may ensure that Investigators establish and maintain ongoing communication with involved caregivers. Periodic re-consent should be considered in some cases. Third party consent monitors may be used during the recruitment and consenting process, or waiting periods may be required to allow more time for the subject to consider the information that has been presented. For subjects with fluctuating decision making capacity or those with decreasing capacity to give consent, a re-consenting process with Health Agent may be necessary.

It is often possible for Investigators and others to enable persons with some decisional impairment to make voluntary and informed decisions to consent or refuse participation in Research. Potential measures include repetitive teaching, group sessions, audiovisual presentations, and oral or written recall tests. Other measures might include follow-up questions to assess subject understanding, videotaping or audio-taping of consent interviews, second opinions, use of independent consent observers, interpreter for hearing-impaired subjects, allowing a waiting period before enrollment, or involvement of a trusted family member or friend in the Disclosure and decision making process.

Although incompetent to provide informed consent, some persons may resist participating in a Research Protocol approved by their representatives. Under no circumstances may subjects be forced or coerced to participate.

In the event Research Participants become incompetent or impaired in decision making capacity after enrollment, the PI is responsible for notifying HRPO. The PI is responsible for developing a monitoring plan which follows the guidelines outlined above for incompetent and impaired decision making Research Participants.

6.10.3 Determining Capacity to Consent

The majority of studies conducted at the University only allow enrolling subjects who have the capacity to consent. For studies that have been approved for enrolling Vulnerable Populations who may lack capacity to consent, there must be someone who is able to assess capacity of each potential subject to consent. The PI may determine after appropriate medical evaluation that the prospective Research subject lacks decision-making capacity and is unlikely to regain it within a reasonable period of time. Additionally, if the reason for lack of capacity is because of mental
illness then a psychiatrist or licensed psychologist must confirm this judgment and document in
the individual’s medical record in a signed and dated progress note.

Decisional capacity in the Research context has been interpreted by the American Psychiatric
Association as requiring:

- Ability to evidence a choice;
- Ability to understand relevant information;
- Ability to appreciate the situation and its likely consequences; and
- Ability to manipulate information rationally.

A range of professionals and methods may be utilized to assess capacity. In general the consent
assessor should be a Researcher or consultant familiar with dementias and qualified to assess and
monitor capacity and consent in such subjects on an ongoing basis. The IRB will consider the
qualifications of the proposed individual(s) and whether he or she is sufficiently independent of
the Research team and/or institution.

A person who has been determined to lack capacity to consent to participate in a Research study
must be notified of that determination before permission may be sought from his or her Legally
Authorized Representative to enroll that person in the study. If permission is given to enroll such
a person in the study, the potential subject must then be notified. If a person objects to
participating, this objection should be respected.

6.10.4 Informed Consent and Assent

Whenever the Participants have the capacity to give consent (as determined by licensed health
care professionals who are qualified to make such determinations consistent with the scope of
their license), informed consent should be obtained and documented in accordance with Section
5 above. When Participants lack the capacity to give consent, PIs may obtain consent from the
Legally Authorized Representative of a subject as described below.

A person who is incompetent or has been determined to lack capacity to consent to participate in
a Research study should be informed about the trial to the extent compatible with the subject’s
understanding and, if possible, the subject should give their Assent to participate, sign and date
the written informed consent or a separate Assent Form (TU Form 401). If the person objects to
participating, this objection should be heeded.

Both PIs and IRB members must be aware that for some subjects, their decision-making capacity
may fluctuate. For subjects with fluctuating decision making capacity or those with decreasing
capacity to give consent, a re-consenting process with Legally Authorized Representative may be
necessary. Although incompetent to provide informed consent, some persons may resist
participating in a Research Protocol approved by their representatives. Under no circumstances
may subjects be forced or coerced to participate.

6.10.5 Consent by Legally Authorized Representative

The regulations generally require that the Investigator obtain informed consent from subjects.
Under appropriate conditions, Investigators also may obtain informed consent from a Legally
Authorized Representative of a subject (Legally Authorized Representative).
This policy is designed to protect Human Subjects from exploitation and harm and, at the same
time, make it possible to conduct essential Research on problems that are unique to persons who
are incompetent, or who have an impaired decision-making capacity.

Legally Authorized Representative may be obtained from a court appointed Legal Guardian of
the person or a Health Agent appointed by the person in a Medical Power of Attorney. For
example, a subject might have designated an individual to provide consent with regard to health
care decisions through a durable power of attorney and have specified that the individual also has
the power to make decisions on entry into Research.
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, an IND 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.
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 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.
\textit{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].

\textit{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 \textit{5 working days} when an Emergency Use Exemption is used (include a completed \textbf{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
contact representatives and make this information available to the IRB at the time of continuing review.

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,
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.

7.5 Investigational Devices in Research

7.5.1 Policy

Use of an Investigational Device in a clinical trial to obtain safety and effectiveness data must be conducted according to FDA’s IDE regulations found at 21 CFR Part 812 and other applicable FDA regulations.

The following procedures describe the use of Investigational Devices in Research Under the Auspices of the Institution’s IRB.

Regulations & Guidelines: FDA 21 CFR 812.00; 21 CFR 812.110; 21 CFR 812.140(a); AAHRPP I.5.B.

7.5.2 Definitions

**Adverse Device Effect (or “ADE”):** is any AE or adverse effect caused by or associated with the use of a Device that is Unanticipated and has not been included in the Protocol or the Investigator’s brochure.

**Device (or Medical Device):** is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related Test Article, including a component part, or accessory which is (a) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in humans, or (b) intended to affect the structure or any function of the body, and which does not achieve any of its primary intended purposes through chemical action within or on the body, and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

**Humanitarian Use Device (“HUD”):** the FDA defines HUD as a Device intended to benefit patients by treating or diagnosing a disease that affects fewer than 4,000 individuals in the U.S. per year. [FDA 21 CFR 814.3(n)].

**Investigational Device:** as defined by the FDA, an Investigational Device is a Device that is the object of a clinical study designed to evaluate the safety or effectiveness of the Device. [21 CFR §812.3(g)]. Investigational Devices include transitional Devices [21 CFR §812.3(r)] that are objects of investigations. However, for the purposes of this document, an Investigational Device may be an approved Device that is being studied for an unapproved use or efficacy.

**Investigational Device Exemption (“IDE”):** is an FDA-approval of the application for an exemption that permits an unmarked Device to be shipped for the purpose of doing Research on the Device. [See 21 CFR §812.1 and §812.2 for the scope and applicability].

**Non-Significant Risk Device (or NSR Device):** is an Investigational Device other than a Significant Risk Device.
**Significant Risk Device ("SR Device"):** is an Investigational Device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a Human Subject;
- Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a Human Subject;
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presented a potential for serious risk to the health, safety, or welfare or a Human Subject;

Otherwise presents a potential for serious risk to the health, safety, or welfare of a Human Subject.

**7.5.3 IDE Requirements:**

The PI must indicate in the **IRB Application** (TU Form 102) whether the Research involves Investigational Drugs or Devices. If so, the PI must indicate if there is an IND/IDE 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/IDE could be a:

- Industry Sponsored Protocol with IND/IDE;
- Letter from the FDA;
- Letter from industry Sponsor; or
- Other document and/or communication verifying the IND/IDE.

For Investigational Devices, NSR Device studies follow abbreviated IDE requirements and do not have to have an IDE application approved by the FDA. If a Sponsor has identified a study as non-significant risk, then the PI must provide an explanation of the determination. If the FDA has determined that the study is non-significant risk, documentation of that determination must be provided.

If the Research involves Drugs or Devices and there is no IND/IDE, the PI must provide a rationale why it is not required.

The IRB will review the application and determine:

- Whether there is an IND/IDE and is so, whether there is appropriate supporting documentation; and
- If the Research involves Drugs or Devices with no IND/IDE, and whether the Research meets the criteria below.

**7.5.4 Exempted IDE Investigations**

For Devices, an IDE is not necessary if:

1. The Research involves a Device, other than a transitional Device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time;
2. The Research involves a Device other than a transitional Device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a Device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of 21 CFR §807 in determining substantial equivalence;

3. The Research involves a diagnostic Device, if the Sponsor complies with applicable requirements in 21 CFR §809.10(c) and if the testing:
   a. Is noninvasive;
   b. Does not require an invasive sampling procedure that presents significant risk;
   c. Does not by design or intention introduce energy into a subject; and
   d. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure;

4. The Research involves a Device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more Devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk;

5. The Research involves a Device intended solely for veterinary use;

6. The Research involves a Device shipped solely for Research on/or with laboratory animals and labeled in accordance with 21 CFR §812.5(c); and/or

7. The Research involves a custom Device as defined in 21 CFR §812.3(b), unless the Device is being used to determine safety or effectiveness for commercial distribution.

7.5.5 Responsibilities

7.5.5.1 Principal Investigator (“PI’)

The PI is responsible for ensuring that the Research is conducted according to all regulatory guidelines, this document, and Institutional policies and procedures. The PI must obtain approval from the IRB before initiating any Research activities or enrolling any subjects in the Research.

The PI proposing the Device Research will be required to provide a plan – to be evaluated by the IRB - that includes storage, security, and dispensing of the Device. Elements of a sound control plan include the following:

1. **Storage**: All Devices received for a study must be stored in a locked environment under secure control with limited access. The area must be within an area of PI’s control. Proper instructions on the use of the Device must be provided to the subjects. A log must be kept regarding the receipt, use, and/or dispensing of the Device and the disposition of remaining Devices at the conclusion of the investigation.

2. **Reporting**: The PI shall report all Unanticipated Problems Involving Risk to Subjects or Others to the IRB according to the procedures outlined in Section 8.

3. **New Device Requirements**: For Research involving investigational new Drugs:
a. If a Device is considered a NSR Device by the PI or Sponsor, but after review the IRB determines the Device to have significant risk, upon receipt of written notice the PI is responsible for notifying the Sponsor of the IRB(s) determination. The PI must provide the IRB with confirmation of this action.

b. If the PI is storing the Devices, he/she must maintain a log indicating the identification/serial number of the Device, name of subject, date dispensed, by whom it was dispensed, and amount remaining.

c. The PI will maintain the following:
   i. Current curriculum vitae (“CV”);
   ii. Protocol of the study;
   iii. Records of receipt and disposition of Devices;
   iv. List of any co-Investigators with their CV;
   v. Certification that all physicians, dentists, and/or nurses responsible in the study have appropriate valid licenses for the duration of the investigation;
   vi. Case Histories with particular documentation on evidence of effects. Emphasis is on safety and possible untoward happenings. All adverse Device effects are reportable;
   vii. IRB letters of approval.
   viii. Device training; and
   ix. Other documents as outlined in the Human Subject Protection Program Standard Operating Procedures.

d. **Logs:**
   i. The **Device Accountability Log** must be completed regarding the receipt, use and/or dispensing of the Device and the disposition of remaining Devices at the conclusion of the investigation; and
   ii. After use, the PI must maintain a log regarding the receipt, use and/or re-dispensing of the Device and the disposition of remaining Devices at the conclusion of the investigation.

e. **Reporting:** The PI will submit to the Sponsor and to the IRB a report of any Unanticipated adverse Device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the Investigator first learns of the effect.

4. **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 these studies are typically called
“investigator initiated studies” when they involve the use 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 the Guidance Document on Requirements of Unsponsored/Investigator-Initiated Research (TU Form 713) and will comply with the regulatory responsibilities 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; and
- 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, 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 University IO.
- The GMP plan has been reviewed and accepted by Tulane’s 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 as part of ongoing Research compliance efforts.

7.5.5.2 IRB

The IRB will review the Research involving Investigational Devices in accordance with the following requirements and the same criteria it would use in considering approval of any Research involving an FDA-regulated product [21 CFR §56.111].

1. Control plan;
2. Unless the FDA has already made a risk determination for the study, the IRB will review NSR Device studies and determine if the Device represents significant or non-significant risk and report the findings to the PI in writing. The IRB will consider the risks and benefits of the Medical Device compared to the risks and benefits of alternative Devices or procedures. NSR Device studies do not require submission of an IDE application but must be conducted in accordance with the abbreviated requirements of IDE regulations. If the study that has been submitted as non-significant risk is considered SR, the IRB may approve the study, but the study cannot begin until an IDE is obtained;
3. The IRB will not review Protocols involving SR Devices under Expedited Review;
4. The IRB will document in the minutes and provide written documentation to the PI of the rationale for determining whether a Device is classified as NSR Device/SR Device; and

5. If the FDA has already made the SR Device or NSR Device determination for the study, the agency’s determination is final and the IRB does not need to make a risk determination.

7.5.6 Emergency Use of Unapproved Medical Devices

An unapproved Medical Device is defined as a Device that is used for a purpose or condition for which the Device requires, but does not have, an approved application for pre-market approval under section 515 of the FDA Act [21 U.S.C. 360(e)]. An unapproved Device may be used in Human Subjects only if it is approved for clinical testing under an approved application for an Investigational Device Exemption (IDE) under section 520(g) of the Act [21 U.S.C. 360(j)(g)] and 21 CFR part 812. Medical Devices that have not received marketing clearance under section 510(k) of the FD&C Act are also considered unapproved Devices which require an IDE.

The FDA recognizes that emergencies arise where an unapproved Device may offer the only possible life-saving alternative, but an IDE for the Device does not exist, or the proposed use is not approved under an existing IDE, or the Investigator/physician or institution is not approved under the IDE. Using its enforcement discretion, FDA has not objected if a physician chooses to use an unapproved Device in such an emergency, provided that the Investigator/physician later justifies to FDA that an emergency actually existed:

- The patient is in a life-threatening condition that needs immediate treatment;
- No generally acceptable alternative for treating the patient is available; and
- Because of the immediate need to use the Device, there is no time to use existing procedures to get FDA approval for the use.

FDA expects the Investigator/physician to determine whether these criteria have been met, to assess the potential for benefits from the unapproved use of the Device, and to have substantial reason to believe that benefits will exist. The Investigator/physician may not conclude that an “emergency” exists in advance of the time when treatment may be needed based solely on the expectation that IDE approval procedures may require more time than is available. Investigator/Physicians should be aware that FDA expects them to exercise reasonable foresight with respect to potential emergencies, and to make appropriate arrangements under the IDE procedures far enough in advance to avoid creating a situation in which such arrangements are impracticable.

In the event that a Device is to be used in circumstances meeting the criteria listed above, the Device developer should notify the Center for Devices and Radiological Health (“CDRH”), Program Operation Staff by telephone (800-638-2041) immediately after shipment is made. [Note: an unapproved Device may not be shipped in anticipation of an emergency.] Nights and weekends, contact the FDA Office of Emergency Operations (HFA-615) 301-443-1240.

The Investigator/physician is required to follow the subject protection procedures as listed below:

- Obtain an independent assessment by an uninvolved physician;
- Obtain informed consent from the patient or a legal representative;
- Notify the IRB; and
- Obtain authorization from the IDE holder, if an approved IDE for the Device exists.

After an unapproved Device is used in an emergency, the Investigator/physician must:

- Report to the IRB within five days [FDA 21 CFR §56.104(c)] and otherwise comply with provisions of the IRB regulations [FDA 21 CFR Part 56];
- Evaluate the likelihood of a similar need for the Device occurring again, and if future use is likely, immediately initiate efforts to obtain IRB approval and an approved IDE for the Device’s subsequent use; and
- If an IDE for the use does exist, notify the Sponsor of the Emergency Use, or if an IDE does not exist, notify FDA of the Emergency Use (CDRH Program Operation Staff 800-638-2041) and provide FDA with a written summary of the conditions constituting the emergency, subject protection measures, and results.

Subsequent Emergency Use of the Device may not occur unless the Investigator/physician or another person obtains approval of an IDE for the Device and its use. If an IDE application for subsequent use has been filed with FDA and FDA disapproves the IDE application, the Device may not be used even if the circumstances constituting an emergency exist. Developers of Devices that could be used in emergencies should anticipate the likelihood of Emergency Use and obtain an approved IDE for such uses.

An exception under FDA regulations at 21 CFR §50.23 permits the Emergency Use of an Investigational Drug, Device, or Biologic without informed consent where the Investigator 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;
- Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
- 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 Investigator 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 HRPO Director (or designee) will review the report to verify that circumstances of the emergency waiver conformed to FDA regulations.

Regulations & Guidelines: FDA 21 CFR §50.23; 21 CFR §50.24; 21 CFR §50.25(d); 21 CFR §56.102(d); 21 CFR §56.104(c); FDA Information Sheets: Emergency Use of an Investigative Drug or Biologics; Emergency Use of Unapproved Medical Devices; AAHRPP I.5.C.
7.5.7 Humanitarian Use Devices (HUD)

Treatment with a HUD is subject to initial Convened IRB Review [FDA 21 CFR §814.124]. At the time of Initial Review the determination may be that Continuing Review meets criteria for Expedited Review. The request for use of a HUD is submitted to the IRB on the HUD Supplement.

If a physician in an emergency situation determines that IRB approval cannot be obtained in time to prevent serious harm or death to a patient, a (HUD) may be Administered without prior IRB approval. In this instance, approval must be obtained from the Vice President for Research and the Investigator is required to provide written notification of the use to the IRB within five days after use of the Device. The IRB requires that written notification include identification (specification without identifiers) of the patient, the date on which the Device was used, and the reason for the use. It is the responsibility of the Investigator to notify the FDA if the IRB were ever to withdraw approval for use of a HUD. The FDA should be notified within five days of notification of the withdrawal of approval. Investigators are reminded that Humanitarian Device Exemptions are for clinical use only and HUD(s) can be used only for purposes outlined in the approved IRB Application (TU Form 102).

8 Unanticipated Problems Involving Risks to Subjects or Others

8.1 Policy

Tulane complies with DHHS and FDA regulations which state that institutions must have written policies on reporting Unanticipated Problems Involving Risks to Subjects or Others (as defined below) to the IRB, institutional officials and relevant Federal agencies and departments.

The following procedures describe how Unanticipated Problems Involving Risk to Subjects or Others are handled in Research under the auspices of HRPO. Refer to HRPO’s Website for the Decision Tree for Reporting Unanticipated Problems to IRB (TU Form 710) to facilitate determining whether a reportable Unanticipated Problem exists.

8.2 Definitions

“Adverse Event” (or “AE”): is any untoward physical or psychological occurrence in a Human Subject participating in Research, including any abnormal sign (e.g., abnormal physical exam or laboratory finding, symptoms or disease associated with the Research or the use of a medical investigational Test Article), symptom, or disease, temporarily associated with the Subject’s participation in the Research. An AE does not necessarily have to have a causal relationship with the Research, or any risk associated with the Research or the Research intervention, or the assessment.

“Others”: means individuals other than Research Participants (e.g., Investigators, research assistants, students, the public, etc.).

Related (or “Possibly Related”): means that there is a reasonable possibility that the event, incident, experience or outcome may have been caused by the procedures involved in the Research, underlying disease, disorder, or condition of the Subject, or other circumstances unrelated to either the Research or any underlying disease, disorder, or condition of the Subject. Note that this is modified from the definition of associated with use of the drug in FDA regulations at 21 CFR §312.32(a). [OHRP 7/15/2007 Guidelines].

Unanticipated Problem Involving Risks to Participants or Others (or “Unanticipated Problem”): means any incident, experience, outcome, or new information where all three elements exist:

1. Is unexpected;
2. Is Related or Possibly Related to participation in the Research, and
3. Indicates that subjects or Others are at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

“Unexpected”: means the incident, experience or outcome is not expected (in terms of nature, severity, or frequency) given the Research procedures that are described in the Protocol-related documents, such as the IRB-approved research Protocol and informed consent documents; and the characteristics of the subject population being studied;

8.3 Procedures

8.3.1 Reporting

Investigators must promptly report the following problems to the IRB:
1. Adverse Events which in the opinion of the PI meet the criteria for an Unanticipated Problem involving risk to subjects or Others.

2. An unanticipated event related to the Research that exposes Participants to potential risk.

3. An unanticipated event related to the Research that exposes individuals other than the research Participants (e.g., Investigators, research assistants, students, the public, etc.) to potential risk.

4. Information that indicates a change to the risks or potential benefits of the Research. For example:
   a. An interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different than initially presented to the IRB.
   b. A paper is published from another study that shows that the risks or potential benefits of your Research may be different than initially presented to the IRB.

5. A breach of confidentiality.

6. Incarceration of a Participant in a Protocol not approved to enroll Prisoners.

7. Change to the Protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research Participant.

8. Complaint of a Participant when the complaint indicates unexpected risks or cannot be resolved by the research team.

9. Protocol violation (meaning an accidental or unintentional change to the IRB approved Protocol) that harmed Participants or Others or that indicates Participants or Others may be at increased risk of harm.

10. Sponsor imposed suspension for risk.

11. Any other event that indicates Participant or Others might be at risk of serious, unanticipated harms that are reasonably related to the Research.

**8.3.2 Submission of Reports**

For Unanticipated Problems at a Tulane site (or at a Non-Tulane Site where Tulane is IRB-of-Record), PIs must report possible Unanticipated Problems to the IRB promptly.

- If the event requires immediate intervention to prevent serious harm to Participants or Others, the PI must report the event within five (5) working days of receiving notice of the event.

- PIs must report all other possible Unanticipated Problems occurring at the Tulane research site and non-Tulane research sites to the IRB as soon as possible but no later than ten (10) working days from the date of the event or from the date of being notified of the event.

For Unanticipated Problems not at a Tulane Site (i.e., external), Tulane’s IRB will accept event reports from a non-Tulane site (e.g., not University or TUHC premises) submitted by Investigators, study sponsors or the FDA on behalf of Investigators, provided the following conditions are met [FDA 21 CFR 312.32]:

138
• Tulane IRB recognizes that for multi-center studies, the Sponsor is in a better position to process and analyze unanticipated event information for the entire study, and to assess whether an occurrence is an Unanticipated Problem for the Study. Accordingly, Investigators may rely on the Sponsor’s assessment and provide the Sponsor’s assessment to the IRB using Tulane’s Unanticipated Problem Report Form (TU Form 607) (together with sponsor-provided reports).

• The IRB will not accept non-Tulane site reports that do not meet Tulane’s reporting requirements.

8.3.3 IRB Procedures for Handling Reports of Possible Unanticipated Problems

8.3.3.1 Review by IRB Staff and Chair

1. Upon receipt of an Unanticipated Event Report Form (TU Form 607) from a PI, the IRB staff checks the form for completeness. If any applicable sections of the form are incomplete or have been answered unsatisfactorily, the IRB staff will contact the PI or the designated contact person to obtain additional information. Corrections are documented in the IRB file, indicating the date, the person spoken with, and the IRB staff making the correction.

2. Upon receipt of a report of a possible Unanticipated Problem from someone other than the Investigator or study staff, the HRPO Director (or designee) will notify the study PI as appropriate for follow-up.

3. The IRB Chair and/or other experienced member(s) designated by the IRB chairperson receives and reviews the report of the event(s) considered to be an Unanticipated Problem and documents his/her findings on the Unanticipated Problems Reviewer Sheet (TU Form 512). The IRB Chair (or designee) will make the final determination as to whether the event is considered an Unanticipated Problem.

4. Based on the information received from the Investigator, the IRB Chair (or designee) may Suspend Research to ensure protection of the rights and welfare of Participants. Suspension directives made by the IRB Chair (or designee) must be reported to a meeting of the Convened IRB.

5. The IRB or the IRB Chair (or designee) has authority to require submission of more detailed information by the PI, the Sponsor, the study coordinating center, or DSMB/data monitoring committee about any AE occurring in a research protocol as a condition of the continuation of the IRB’s approval of the Research.

6. If the reviewer considers that either (1) the problem was foreseen; OR (2) no Participants or Others were harmed AND Participants or Others are not at increased risk of harm, the reviewer should indicate on the Unanticipated Problem Report Form (TU Form 607) that the problem is not an Unanticipated Problem. The form is filed in the protocol record, the determination is communicated to the PI and no further action is taken.

7. If the reviewer considers that the problem is an Unanticipated Problem, but that the risk is no more than minimal, the reviewer will review:

   • The currently approved protocol
   • The currently approved consent document
   • Previous reports of Unanticipated Problems
The Investigator’s Brochure, if one exists

After reviewing all of the materials, the reviewer will take appropriate action depending on the nature of the risk involved, including modification of the protocol or the consent form, if applicable. The results of the review will be recorded in the protocol record, communicated to the PI, and reported to the IRB. All events determined to be Unanticipated Problems will be reported to the IRB (see Section 9) and to relevant regulatory agencies and institutional officials according to the procedures in Section 11.

8. All reported Unanticipated Problems where the risk is more than minimal will be reviewed at a Convened IRB meeting.

8.3.3.2 IRB Review

The primary reviewer will be given the protocol file, the currently approved consent document, previous reports of Unanticipated Problems, the Investigator’s Brochure (if one exists), the event report, and recommendations from the IRB Chair (or designee), when appropriate. All IRB members will receive the event report.

After review of the protocol and event report, the convened IRB will make findings and recommendations based on the following considerations:

a. Whether the reported event is an Unanticipated Problem according to the definition in this policy.

b. What action in response to the report is appropriate.

c. Whether suspension or termination of approval is warranted.

d. Whether further reporting to Institutional and/or Federal officials is required.

1. If the IRB finds that the event is not an Unanticipated Problem, according to the definition in the policy, the IRB may recommend any of the following actions:

a. No action

b. Requiring modifications to the protocol

c. Revising the continuing review timetable

d. Modifying the consent process

e. Modifying the consent document

f. Providing additional information to current Participants (e.g. whenever the information may relate to the Participant’s willingness to continue participation)

g. Providing additional information to past Participants

h. Requiring additional training of the investigator and/or study staff

i. Other actions appropriate for the local context

2. If the IRB finds that the event is an Unanticipated Problem, according to the definition in the policy, the IRB may recommend any of the following actions:

a. Requiring modifications to the Protocol
b. Revising the continuing review timetable

c. Modifying the consent process

d. Modifying the consent document

e. Providing additional information to current Participants (e.g. whenever the information may relate to the Participant’s willingness to continue participation)

f. Providing additional information to past Participants

g. Requiring additional training of the investigator and/or study staff

h. Reconsidering approval

i. Requirement that current Participants re-consent to participation

j. Monitoring of the Research

k. Monitoring of the consent

l. Referral to other organizational entities (e.g., Office of General Counsel, RCO, Risk Management, IO, etc.)

m. Suspending the Research

n. Terminating the Research

o. Other actions appropriate for the local context

3. If a report suggests that Participant safety is at risk, the IRB may immediately Suspend or Terminate the Research. Any suspension or termination of Research by the IRB must be promptly reported to the VPR, and OHRP, and FDA (if FDA-regulated research) through the VPR. This should be done in writing.

4. If, after reviewing a report, the IRB finds that the event is an Unanticipated Problem or that Suspension or Termination of approval is warranted, the IRB will:

a. Notify the investigator in writing of its findings, with copies to the Chair of the Investigator’s department and/or research unit, and the Investigator’s supervisor, and

b. Report its findings and recommendations to the VPR for further reporting to the appropriate Federal officials (e.g., OHRP or FDA).
9 Protocol Violations, Deviations, and Exceptions

9.1 Definitions

Protocol Deviation(s): means a minor or administrative departure from the IRB-approved Protocol procedures (e.g., the Protocol, informed consent document, recruitment process or study materials) that was made without prior sponsor and IRB approval. It is an accidental or unintentional change to, or non-compliance with the Research Protocol that neither (a) increases the risk or decreases the benefit; and (b) significantly affects the subject’s rights, safety or welfare and/or the integrity of the Research data. [Not defined by Common Rule or FDA regulations].

Protocol Exception (or “Exception”): means an impermanent (temporary) Protocol deviation that is pre-approved by the sponsor or funding agency, (and the FDA, if applicable, for investigational device studies) and the IRB prior to its implementation. Protocol Exceptions are generally for a single subject (e.g., the patient/subject is allergic to one of the medications provided as supportive care) or, occasionally, a small group of subjects. The Protocol Exception is usually evaluated by both the sponsor or funding agency (and FDA, if applicable) and the IRB in order to determine that it does not increase the risk to the subject(s), or jeopardize the integrity of the research data. Documentation of sponsor (or FDA) pre-approval and IRB approval of the exception should be maintained in the investigator’s research study file.

Protocol Violation(s): means an accidental or unintentional change to, or non-compliance with the IRB-approved procedures (e.g., the Protocol, informed consent document, recruitment process or study materials) without prior sponsor and IRB approval. Protocol Violations generally increases risk and/or decrease the benefit; affect the subject’s rights, safety or welfare and/or the integrity of the Research data. This term is not defined by the Common Rule or FDA regulations.

9.2 Planned Changes to Research Protocol

With regard to planned changes to a Research Protocol, the most common occurs through the submission of an amendment. Examples include an increase in subject number, changes in Investigators or key personnel, a change to the funding source, changes in procedures, revised consent documents and revised HIPAA Authorization. These all involve planned changes through an amended Protocol and are not Protocol Deviations themselves (although they may result from a Protocol Deviation).

Another type of planned change to the Research is called a Protocol Exception, which is made for a single subject or a small group of subjects, but is not a permanent revision to the research Protocol. Protocol Exceptions are a subset of Protocol Deviations. Similar to an amendment, a Protocol Exception must be IRB approved prior to its implementation. If the Research involves an investigational Agent (e.g., Drug, Device, or Biologic), except in an emergency situation to eliminate immediate harm, prior approval by the sponsor also is required. Additionally, when Research involves an Investigational Device and the changes or deviations may affect the scientific soundness of the Research plan or rights, safety, or welfare of subjects, FDA and IRB pre-approval is required [21 CFR §812.150(4)]. Although a Protocol Exception must be prospectively approved by IRB, because the change does not involve a permanent change to the research Protocol, the FDA considers it to represent a Protocol Deviation.
Another type of planned change to a Protocol is a change made to eliminate apparent immediate harm to a subject. This type of change can be initiated without prior IRB approval, provided that subsequent IRB approval is obtained. These planned changes are a subset of Protocol Deviations.

9.3 Unplanned Changes to Research Protocol

The next category involves unplanned changes to a Research Protocol not otherwise approved by the IRB. Such unplanned changes are either Protocol Deviations or Protocol Violations. These unplanned changes may include changes of the IRB-approved Research Protocol, Good Clinical Practice (GCP) guidelines, regulatory standards, or Tulane’s HRPP.

9.4 Protocol Deviations:

A Protocol Deviation is any change or alteration from the procedures stated in the study Protocol, consent document, recruitment process, or study materials (e.g. questionnaires) originally approved by the IRB (but the change or alteration itself is not IRB-approved). Protocol Deviation is a general term and includes, Protocol Exceptions, changes made to avoid immediate harm to subjects, and Protocol Violations. [45 CFR §46.103 (b) (4) (iii), 21 CFR §56.108 (a) (4)]. Protocol Deviations can be either major or minor. Protocol Deviations can be examples of non-compliance, either non-serious or serious.

Repeated failure by a PI to not report Protocol Deviations may be viewed as non-compliance with the Federal regulations, the guidelines that govern ethical conduct of Research, and Tulane’s HRPP.

9.5 Protocol Violation:

A Protocol violation (“Protocol Violation”) is a subset of Protocol Deviation. It is any planned or unintended change or deviation from the IRB approved study Protocol, consent document, recruitment process, or study materials that were not approved by the IRB prior to implementation. Generally, Protocol Violations occur after the subject is enrolled in the Research. However, some Protocol Violations, such as deviations from the approved consent process, can occur before the subject is enrolled in the research. Protocol Violations may be either Major Protocol Violations or Minor Protocol Violations, based on their relative severity.

9.6 Major Protocol Violation:

A major Protocol violation (“Major Protocol Violation”) is a deviation that has an impact on subject safety, may substantially alter risks to subjects, may have an effect on the integrity of the study data, or may affect the subject’s willingness to participate in the study. Major Protocol Violations can vary in the degree of seriousness according to how the changes impact subject safety, the degree of non-compliance with Federal regulations, State laws, the HRPP, Tulane policies or procedures, and the degree of foreknowledge of the event.

All Major Protocol Violations must be reported by the PI to the IRB within five (5) working days of learning of the violation. Use the Protocol Deviation/Violation/Exception Form (TU Form 606) to report Major Protocol Violations. If it is necessary to make a permanent change to the study procedures in order to avoid harm to other subjects, then a Protocol amendment should be submitted as soon as possible by the PI, using an Application for Amendment (TU Form 601). If appropriate to maintain safety of the subjects, new subject enrollment should be temporarily stopped by the PI until the amendment is approved.
No matter who discovers a Major Protocol Violation (e.g., sponsor or their agent during a monitoring visit), the PI is responsible for reporting it to the IRB.

**Example of Major Protocol Violations:**

- Failure to obtain valid informed consent (e.g., verbal consent obtained rather than IRB-required signed informed consent);
- Enrolling a subject who does not meet the inclusion and exclusion criteria;
- Use of recruitment procedures that have not been approved by the IRB;
- Continuing Research activities after IRB approval has expired;
- Any deviations from the investigational plan for an Investigational Device taken to protect the life or physical well-being of a Participant in an emergency;
- Any Emergency Use of an FDA-regulated Test Article or Humanitarian Use Device (HUD) prior to IRB approval;
- Hospitalization or death of subject participating in human gene transfer/gene therapy Protocol;
- Hospitalization or death caused/contributed by a HUD;
- Protocol Deviations taken without prior IRB review to eliminate an apparent immediate hazard to Subjects;
- Any event that requires prompt reporting to the Sponsor;
- Failure to perform a required laboratory test or procedure that could impact upon the safety of the subject;
- Sponsor-imposed suspension for risk;
- Breaches in subject confidentiality or privacy that could pose an increased risk to subjects or others;
- An Investigator deliberately decides to follow a different procedure than that set forth in the Protocol for one or more subjects (other than to eliminate apparent immediate hazards to the subject or others);
- Loss of laptop computer that contained identifiable, private information about subjects;
- Accidental distribution of incorrect study medication;
- Investigator realizes that a diagnostic blood test was not described in the Protocol but is needed to regulate serum levels of the study Drug;
- The Protocol indicates that a research nurse will conduct in-take interviews and review the consent document with subjects. The research nurse retires, so a non-study clinic nurse does the procedure instead;
- Sponsor believes that study data to date indicates a potential subject could safely participate but does not meet currently approved eligibility criteria (Protocol Exception).

**Planned** Protocol Deviations (e.g., enrolled subjects).

Refer to **IRB Reporting Guidelines for Protocol Deviations/Violations/Exceptions** (TU Form 704) or **Decision Tree for Reporting Violations/Deviations/Exceptions to IRB** (TU Form 709), which can be found on HRPO’s Website.

### 9.7 Minor Protocol Violation:

A Minor Protocol Violation is one that does not impact subject safety, compromise the integrity of the study data, or affect the subject’s willingness to participate in the study.
No matter who discovers a Minor Protocol Violation (e.g., sponsor or their agent during a monitoring visit), the PI is responsible for reporting it to the IRB.

All Minor Protocol Violations do not require prompt reporting and should be reported by the PI to the IRB within ten (10) working days (or no later than at the time of continuing review) of learning of the violation. Use the Protocol Deviation/Violation/Exception Form (TU Form 606) to report Minor Protocol Violations.

### Example of Minor Protocol Violations:

- Research study visits occurring outside of study window not impacting subject safety or Research data;
- A rescheduled study visit;
- Enrollment numbers that exceed specifications;
- Missed study procedures not causing an increased risk to subjects or adversely affecting the study data;
- Incarceration of a Participant enrolled in a Protocol not approved to enroll Prisoners;
- Failure to collect an ancillary self-report questionnaire;
- Use of unapproved recruitment procedures or materials (e.g., when slightly altered);
- Inappropriate consent process documentation (e.g., dated by someone other than the subject, missing signature of person obtaining consent, incorrect date on consent);
- Use of expired or outdated consent document (i.e., it does not affect the safety of the subject, integrity of the study, or subject’s willingness to participate in the Research);
- Study visits outside the Protocol-prescribed visit window (e.g., the subject is on vacation or is 1 week late for a visit due to illness);
- Failure of the subject to return unused study medication; and
- Subject’s refusal to complete scheduled Research activities, not adversely affecting subject or Research data.

Refer to IRB Reporting Guidelines for Protocol Deviations/Violations/Exceptions (TU Form 704) or Decision Tree for Reporting Violations/Deviations/Exceptions to IRB (TU Form 709), which can be found on HRPO’s Website.

### 9.8 Protocol Exception:

A Protocol Exception is an impermanent (temporary) Protocol Deviation that is reapproved by the sponsor or funding agency, (and, if applicable, the FDA for Investigational Device studies) and the IRB, prior to its implementation. Protocol Exceptions are generally for a single subject or, occasionally, a small group of subjects.

Protocol Exceptions must be submitted to IRB and granted approval prior to subject enrollment and implementation, except where necessary to eliminate apparent immediate hazards to the Human Subjects. [DHHS 45 CFR §46.103(b)(4); FDA 21 CFR §56.108(a)(4); ICH 3.3.7].

The Protocol Exception is usually evaluated by both the sponsor or funding agency (and the FDA, if applicable) and the IRB in order to determine that it does not increase the risk to the subject(s), or jeopardize the integrity of the research data. Documentation of sponsor (or FDA) pre-approval and IRB approval of the exception should be maintained in the PI’s Research Records. If the Research involves an Investigational Device, and the changes or deviations may
affect the scientific soundness of the plan or the rights, safety, or welfare of the Human Subjects, FDA pre-approval is also required [21 CFR §812.150 (4)].

The PI has ultimate responsibility for obtaining prior IRB approval for Protocol Exceptions. Repeated failure to obtain prospective IRB approval for Protocol Exceptions may be viewed as non-compliance with the Federal regulations, the guidelines that govern ethical conduct of Research, and Tulane’s HRPP.

### Example of Protocol Exceptions:

- Enrollment of a Research subject who fails to meet all of the Protocol eligibility criteria (e.g., the subject may have been evaluated for all other parameters, and it was determined that not meeting this inclusion criteria or laboratory screening value would not cause harm to the subject or alter the validity of the study)

Refer to IRB Reporting Guidelines for Protocol Deviations/Violations/Exceptions (TU Form 704) or Decision Tree for Reporting Violations/Deviations/Exceptions to IRB (TU Form 709), which can be found on HRPO’s Website.

#### 9.9 IRB Review Process

##### 9.9.1 Protocol Deviations

Major Protocol violations that occur in research that involves greater than minimal risk (originally reviewed and approved by the convened IRB) must be submitted for convened review. Major Protocol violations that occur in research that involves minimal risk (originally reviewed and approved via expedited review procedures, or determined by the convened IRB to meet expedited review criteria) may be eligible for expedited review. The IRB Chair or designee will review the violation and determine whether it should be reviewed via expedited or requires convened IRB review. All major Protocol violations that occurred since the initial or most recent continuing review should be summarized in the appropriate section of the continuing review form. Alternatively, copies of the report forms submitted to the IRB may be attached to the Application for Continuing Review (TU Form 603).

##### 9.9.2 Major Protocol Violations

Investigators reporting Major Protocol Violations must complete a Protocol Deviation/Violation/Exception Form (TU Form 606). Each Protocol violation report should discuss what measures have been put in place to prevent future re-occurrences of the same event. The PI should also evaluate Protocol violations for any trends or patterns that would require additional corrective actions or submission of a Protocol amendment to prevent future violations. Repeated violations of a similar nature may be a clear indication that a permanent change (i.e. an amendment) to the study procedures is necessary.

The event is logged in by HRPO staff, and entered into the HRPO database system as a Protocol Violation. The HRPO Director, HRPO Assistant Director, or Coordinator for the relevant IRB will pre-review the submission for completeness and determines the level of review required.

The IRB member review will be documented on the Protocol Deviation Reviewer Sheet (TU Form 511). If the IRB reviews the event via Expedited Review, the assigned IRB reviewer will
document the review on the same review guide. The possible determinations the IRB reviewer may make about the event through expedited review are as follows:

- **Acknowledged** - no further information or action required’
- **Modifications or Additional Information Required** – Additional information is needed in order to appropriately evaluate the event or changes to the Research that are minor in nature are being required based upon the event;
- **Refer for Convened Review** – If the HRPO staff determine the event is not eligible for Expedited Review or the IRB member prefers that the event be reviewed by the convened IRB. Additional information or materials may also be requested. If there are safety issues or concerns related to the event, the IRB may make additional determinations as described below for convened review;
- **Terminate the Research**; and
- **Refer events or concerns regarding the research for non-compliance review to the University RCO.**

For Protocol Violations that require Fully Convened IRB Review, the assigned IRB member reviewers would document determinations on the **Protocol Deviation Reviewer Form** (TU Form 511). The potential determinations are as follows:

- **Acknowledged** - no further information or action required;
- **Modifications or Additional Information Required** – Additional information is needed in order to appropriately evaluate the event or changes to the research that are minor in nature are being required based upon the event;
- **If there are safety issues or concerns related to the event** the IRB may make additional determinations that include, but are not limited to, the following:
  - Require Substantive changes of the research Protocol and/or informed consent document including the re-consenting of previously enrolled subjects;
  - Implement additional safeguards, such as additional safety monitoring or more frequent safety monitoring;
  - Increase the continuing review frequency (i.e. 6 months or 3 months);
  - Suspend the research and recommend revisions to the research that must be made before the suspension can be lifted;
  - Suspend enrollment of new subjects, either temporarily or permanently;
  - Discontinue the participation of currently enrolled subjects;
  - Terminate the research;
  - Refer events or concerns regarding the research for non-compliance review to the University RCO.

For Federal reporting, purposes the IRB will need to determine whether the Protocol Violation constitutes an instance of serious or Continuing Non-Compliance. If the violation is an event involving a change in the Protocol to eliminate immediate hazard or harm to subjects, the IRB should ensure that the event was reported in the required 5-day period. Also, the IRB should make certain that the PI implemented appropriate measures to alleviate or eliminate the harm to current and future subjects in the Research.

For Protocol Violations reviewed via Expedited Review, the IRB reviewer documents his/her determination on the **Protocol Deviation Reviewer Form** (TU Form 511). If the Protocol
Violation is reviewed by a Fully Convened IRB, the primary reviewers document their initial determinations regarding the Protocol Violation on the Protocol Deviation Reviewer Form (TU Form 511). The Fully Convened IRB discusses the event at the convened meeting and the IRB meeting minutes document the discussion and final determination of the convened IRB regarding the Protocol Violation. The documentation of review is placed in HRPO’s Protocol file. Once a determination is made by the IRB, the PI will receive a notification of determination from the IRB. If there are no issues with the Protocol violations, the PI will receive an Acknowledgement of Protocol Violation.

9.9.3 Minor Protocol Violations

Each Protocol violation report should discuss what measures have been put in place to prevent future re-occurrences of the same event. The PI should also evaluate Protocol violations for any trends or patterns that would require additional corrective actions or submission of a Protocol amendment to prevent future violations. Repeated violations of a similar nature may be a clear indication that a permanent change (i.e. an amendment) to the study procedures is necessary.

Minor Protocol violations do not require prompt reporting and should be reported with (10) working days of the violation, and may be reported to the IRB in summary form at the time of next continuing review. All Protocol violations should be reported to the research sponsor or funding agency in a timely fashion and according to that company’s or agency’s policy. All Protocol violations should be documented in the investigator’s research study files.

Tulane investigators are not required to report Protocol violations to Tulane’s IRB that occur at other research sites in multi-center research trials. The Investigator may have other reporting requirements such as reporting to Tulane University Health Center, Medical Center of Louisiana/LSU New Orleans, the Clinical Translational Research Center, Institutional Biosafety Committee, and/or other appropriate institutional entities that are not covered in this policy.

It is highly recommended that the Investigator keep a log of Protocol violations for each research study. The log should include the subject study identifier, the date of the violation, an indication of whether the violation was a major or minor violation, a description of the violation, the date of the IRB submission, date of notification from the IRB, date of sponsor notification, and the date of sponsor notification of receipt. Copies of the report sent to the IRB should also be maintained in the research files.

9.9.4 Protocol Exceptions:

Investigators requesting a Protocol Exception must complete a Protocol Deviation Reviewer Form (TU Form 511) and submit the form to Tulane’s HRPO with any supporting documentation. The Protocol Exception is processed within HRPO. The submission is logged in at the front desk, and entered into the HRPO database system as a Protocol Deviation. The HRPO Director, HRPO Assistant Director, or Coordinator for the relevant IRB will pre-review the submission for completeness and determines the level of review required.

Protocol Exceptions can be reviewed either through expedited or convened procedures depending upon the type of Research and nature of the exception request. If the exception requires Fully Convened IRB Review, the HRPO Director, HRPO Assistant Director, or Coordinator schedules the Protocol Exception for an IRB meeting agenda. The pre-review and any subsequent IRB member review is documented using the Protocol Deviation Reviewer Form (TU Form 511).
The IRB members reviewing the Protocol Exception via Expedited Review procedures or the primary reviewers assigned to review the exception at a Fully Convened IRB meeting, as well as all members of the convened IRB, will have access to the full Protocol file, which includes the current version of the research Protocol. The possible determinations IRB members can make regarding exceptions include:

- Exception approved – no issues;
- Expedited review (as determined by IRB Chair (or designee));
- Modifications required;
- Referred for Fully Convened IRB Review;
- Disapproval (use only for Fully Convened IRB Review);
- Deferral- further justification or information required (use only for Fully Convened IRB Review);
- Deferred to University RCO (as determined by IRB Chair (or designee), or Fully Convened IRB).

For Protocol Exceptions reviewed via Expedited Review, the IRB reviewer documents their determination on the review guide. If the Protocol Exceptions are reviewed at a convened IRB meeting, the primary reviewers document their initial determinations regarding the Protocol Exceptions on the review guide. The Fully Convened IRB discusses the event at the convened meeting and the IRB meeting minutes document the discussion and final determination of the Fully Convened IRB regarding the Protocol Exceptions. The documentation of review is placed in the HRPO Protocol file.

Once a determination is made by the IRB, the PI will receive a notification of determination from the IRB.

Regulations & Guidelines: DHHS 45 CFR §46.103(b)(4)(iii); FDA 21 CFR §56.108(a)(4); 21 CFR §56.108(b); 21 CFR §812.150.
10 Complaints and Non-compliance

10.1 Policy

As part of its commitment to protecting the rights and welfare of Human Subjects in Research, Tulane reviews all complaints and allegations of Non-Compliance and takes any necessary action to ensure the ethical conduct of Research.

All Investigators and other study personnel involved in Human Subjects Research are required to comply with all laws and regulations governing their Research activities, as well as with requirements and determinations of the IRB. Study personnel include the Principal Investigator and any staff member directly involved with Participants or the informed consent process.

The following procedures describe how complaints and allegations of Non-Compliance are handled by the IRB. In cases where Serious Non-Compliance or Continuing Non-Compliance has occurred, the IRB may exercise its authority to monitor, Suspend, or Terminate the Research.

Regulations & Guidance: DHHS 45 CFR §46.103(b)(5)(i); 45 CFR §46.116(b)(5); FDA 21 CFR §50.25(b)(5); 21 CFR §56.108(b)(2); OHRP Guidance on Reporting Incidents to OHRP.

10.2 Definitions

**Allegation of Non-Compliance**: is defined as an unproved assertion of Non-Compliance.

**Continuing Non-Compliance**: is defined as a pattern of Non-Compliance that, in the judgment of the RCO or convened IRB, suggests a likelihood that instances of non-compliance will continue without intervention. Continuing Non-Compliance also includes failure to respond to a request to resolve an episode of Non-Compliance.

**Finding of Non-Compliance**: is an Allegation of Non-Compliance that is proven true or a report of Non-Compliance that is clearly true. (e.g., a finding on an audit of an unsigned consent document, or an admission of an Investigator that the Protocol was willfully not followed would represent reports of non-compliance that would require no further action to determine their truth and would therefore represent findings of Non-Compliance.)

**Non-Compliance**: is a failure to comply with any of the regulations and policies described in this document and failure to follow the determinations of the IRB. Non-Compliance may be minor or sporadic or it may be serious or continuing.

**Serious Non-Compliance**: is the failure to follow any of the regulations and policies described in these SOPs or failure to follow the determinations of the IRB and which, in the judgment of the convened IRB, increases risks to Participants, decreases potential benefits, or compromises the integrity of the HRPP. Research being conducted without prior IRB approval is considered Serious Non-Compliance.

10.3 Complaints

The IRB Chair will promptly handle (or delegate staff to handle), and, if necessary, investigate all complaints, concerns, and appeals received by the IRB. This includes complaints, concerns, and appeals from Investigators, Research Participants and others.

All complaints, written or verbal (including telephone complaints), and regardless of point of origin, are recorded on the Concerns and Complaint (TU Form 604) and forwarded to the IRB Chair and HRPO Director.
Upon receipt of the complaint, the IRB Chair will make a preliminary assessment whether the complaint warrants immediate Suspension of the Research project. If a Suspension is warranted, the procedures in Section 3.11.1 will be followed.

If the complaint meets the definition of Non-Compliance, it will be considered an Allegation of Non-Compliance according to Section 10.4.

If the complaint meets the definition of an Unanticipated Problem, it will be handled according to Section 8.

Within 10 business days of receipt of the complaint, the IRB Chair and/or HRPO Director shall generate a letter to acknowledge that the complaint has been received and is being investigated, providing a follow-up contact name.

10.4 Non-Compliance

Investigators and their study staff are required to report instances of possible Non-Compliance. The PI is responsible for reporting any possible Non-Compliance by study personnel to the IRB. Common reports to the IRB that are not serious or continuing are typically Protocol Violations. However, any individual or employee may report observed or apparent instances of non-compliance to the Tulane IRB. In such cases, the reporting party is responsible for making these reports in good faith, maintaining Confidentiality and cooperating with any IRB and/or Institutional review of these reports.

If an individual, whether Investigator, study staff or other, is uncertain whether there is cause to report non-compliance, he or she may contact the IRB Chair (or designee) directly to discuss the situation informally.

Reports of Non-Compliance must be submitted to the HRPO within 10 working days of discovery of this non-compliance. The report must include a complete description of the non-compliance, the personnel involved and a description of the Non-Compliance.

Regulations & Guidance: FDA 21 CFR §56.108(b).

10.4.1 Review of Allegations of Non-Compliance

All allegations of Non-Compliance will be reviewed by HRPO or RCO, who will review:

1. All documents relevant to the allegation
2. The last approval letter from the IRB
3. The last approved IRB Application (TU Form 102) and Protocol;
4. The last approved Consent (TU Forms 402, 403) document
5. The grant, if applicable; and
6. Any other pertinent information (e.g., questionnaires, DSMB reports, etc.).

Persons conducting audits should use the Audit Form for IRB Approved Protocols (TU Form 204).

The reviewer will review the allegation within 10 working days and make a recommendation following the review as to the truthfulness of the allegation (unless additional time is granted to conduct the review by the IRB Chair).
When a recommendation of Non-Compliance is made because the incident was within the limits of an approved Protocol for the Research involved, the determination is reported by the IRB in writing to the PI following the review and, if applicable, the reporting party.

If in the judgment of the IRB, any allegation or Findings of Non-Compliance is considered true, the Non-Compliance will be processed according to Section 10.4.2.

If in the judgment of the IRB, any allegation or Findings of Non-Compliance warrants Suspension of the Research before completion of any review or investigation to ensure protection of the rights and welfare of Participants, the IRB Chair (or designee) may Suspend the Research as described in Section 3.11 with subsequent review by the IRB Committee.

The IRB Chair (or designee) may determine that additional expertise or assistance is required to make these determinations and may form an ad hoc committee to assist with the review and fact gathering process. When an ad hoc committee assists in the review process, the Chair (or designee) is responsible for assuring that minutes of the meeting are generated and kept to help support any determinations or findings made by the ad hoc committee.

**10.4.2 Review of Findings of Non-Compliance**

**10.4.2.1 Non-compliance is not Serious or Continuing:**

When the IRB determines that Non-Compliance occurred, but the Non-Compliance does not meet definition of Serious Non-Compliance or Continuing Non-Compliance, the determination is reported in writing to the PI and if applicable the reporting party. The RCO (or designee) will work with the PI to develop a corrective action plan to prevent future Non-Compliance. The report of Non-Compliance and corrective action is reported to the IRB through the Expedited Initial Submission Reviewer Sheet (TU Form 509), and reflected in the IRB minutes. If however, the PI refuses to cooperate with the corrective action plan, the matter is referred to a convened meeting of the IRB with notification to the IO and HRPO Director.

**10.4.2.2 Serious Non-Compliance or Continuing Non-Compliance**

When the IRB Chair (or designee) determines that Non-Compliance has occurred and that the Non-Compliance meets the definition of Serious Non-Compliance or Continuing Non-Compliance, the report of Non-Compliance is referred for review by the IRB at the next convened available meeting. However, the IRB Chair (or designee) may use discretion and call an emergency IRB meeting should the circumstances warrant such an urgent meeting.

Examples of Serious Non-Compliance may include the following: falsifying IRB documents; conducting Human Subjects Research without IRB approval; deviating from the IRB-approved Protocol or consent process; modifying the Protocol or consent process without prior IRB approval.

All findings of serious or Continuing Non-Compliance referred to the IRB will be reviewed at a convened meeting. All IRB members will receive:

- All documents relevant to the allegation
- The last approval letter from the IRB
- The last approved IRB Protocol; and
- The last approved consent document.
At this stage, the IRB may:

- Find that there is no issue of Non-Compliance
- Find that there is Non-Compliance that is neither Serious Non-Compliance nor Continuing Non-Compliance and an adequate corrective action plan is in place
- Find that there is serious or Continuing Non-Compliance and approve any changes proposed by the IRB Chair and/or ad hoc committee
- Find that there may be serious or Continuing Non-Compliance and direct that a formal inquiry (described below) be held; or
- Request additional information.

10.4.3 Inquiry Procedures

A determination may be made by the IRB that an inquiry is necessary based on several issues that may include but are not limited to:

1. Subjects' complaint(s) that rights were violated;
2. Report(s) that Investigator is not following the Protocol as approved by the IRB;
3. Unusual and/or unexplained AEs in a study;
4. Repeated failure of Investigator to report required information to the IRB.

A subcommittee is appointed consisting of IRB members, and non-members if appropriate, to ensure fairness and expertise. The subcommittee is given a charge by the IRB, which can include any or all of the following:

1. Review of Protocol(s) in question;
2. Review of Sponsor audit report of the Investigator, if appropriate;
3. Review of any relevant documentation, including consent documents, case report forms, subject's investigational and/or medical files etc., as they relate to the Investigator's execution of her/his study involving Human Subjects;
4. Interview of appropriate personnel if necessary;
5. Preparation of either a written or oral report of the findings, which is presented to the Convened IRB at its next meeting;
6. Recommend actions if appropriate.

10.4.4 Final Review

The results of the inquiry will be reviewed at a convened IRB meeting where the IRB will receive a report from the subcommittee. If the results of the inquiry substantiate the finding of serious or Continuing Non-Compliance, the IRB’s possible actions could include, but are not limited to:

1. Request a correction action plan from the Investigator
2. Verification that Participant selection is appropriate and observation of the actual informed consent
3. An increase in data and safety monitoring of the Research activity
4. Request a directed audit of targeted areas of concern
5. Request a status report after each Participant receives intervention
6. Modify the Continuing Review cycle
7. Request additional Investigator and staff education
8. Notify current subjects, if the information about the Non-Compliance might affect their willingness to continue participation
9. Require modification of the Protocol
10. Require modification of the information disclosed during the consent process
11. Require current Participants to re-consent to participation
12. Suspend the study (See below)
13. Terminate the study (See below)

In cases where the IRB determines that the event of Non-Compliance also meets the definition of Unanticipated Problem, the policy and procedure for review of such events will also be followed. The Investigator is informed of the IRB determination and the basis for the determination in writing and is given a chance to respond. If the IRB determines that the Non-Compliance was serious or continuing, the results of the final review will be reported as described below in Section 11.
11 Reporting to Regulatory Agencies and Institutional Officials

11.1 Policy
Federal regulations require prompt reporting to appropriate institutional officials, and the department or agency head of (i) any Unanticipated Problem or any Serious Non-Compliance or Continuing Non-Compliance with this policy or the requirements or requirements or determinations of the IRB; and (ii) any Suspension or Termination of IRB approval. The HRPO will comply with this requirement and the following procedures describe how these reports are handled.

11.2 Procedures
1. IRB staff will initiate these procedures as soon as the IRB takes any of the following actions:
   a. Determines that an event may be considered an Unanticipated Problem
   b. Determines that Non-Compliance was serious or continuing
   c. Suspends or Terminates approval of Research
2. The HRPO Director (or designee) is responsible for preparing reports or letters which includes the following information:
   a. The nature of the event (Unanticipated Problem Involving Risks to Subjects or Others, Serious or Continuing Non-Compliance, Suspension or Termination of approval of Research)
   b. Name of the Institution conducting the Research
   c. Title of the Research project and/or grant Proposal in which the problem occurred
   d. Name of the Principal Investigator on the Protocol
   e. Number of the Research project assigned by the IRB and the number of any applicable Federal award(s) (grant, contract, or cooperative agreement)
   f. A detailed description of the problem including the findings of the organization and the reasons for the IRB’s decision
   g. Actions the Institution is taking or plans to take to address the problem (e.g., revise the Protocol, Suspend subject enrollment, Terminate the Research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.)
   h. Plans, if any, to send a follow-up or final report by the earlier of
      i. A specific date
      ii. When an investigation has been completed or a corrective action plan has been implemented
3. The IRB Chair, HRPO Director, and the IO will review the letter and modify the letter/report as needed.
4. The IO is the signatory for all correspondence from the facility.
5. The Director (or designee) sends a copy of the report to:
   a. The IRB by including the letter in the next agenda packet as an information item
   b. The IO
   c. The following Federal agencies:
      d. OHRP, if the study is subject to DHHS regulations or subject to a DHHS Federal-wide Assurance
      e. FDA, if the study is subject to FDA regulations.
      f. If the study is conducted or funded by any Federal Agency other than DHHS that is subject to “The Common Rule”, the report is sent to OHRP or the head of the agency as required by the agency
         Note: Reporting to a regulatory agency is not required if the event occurred at a site that was not subject to the direct oversight of the organization, and the agency has been notified of the event by the Investigator, Sponsor, another organization, or other mechanisms.
   g. Principal Investigator
   h. Sponsor, if the study is Sponsored
      i. Contract Research Organization ("CRO"), if the study is overseen by a contract Research Organization
      j. Department Head or supervisor of the PI
      k. Others as deemed appropriate by the IO

The HRPO Director ensures that all steps of this policy are completed within 10 working days of the initiating action. For more serious actions, the Director will expedite reporting.
12 **Investigator Responsibilities**

12.1 **Policy**

PIs are ultimately responsible for the conduct of Research. Research must be conducted according to the signed Investigator statement, the investigational plan and applicable regulations for protecting the rights, safety, and welfare of subjects under the PI(s) care. PIs may delegate Research responsibility. However, Investigators must maintain oversight and retain ultimate responsibility for the conduct of those to whom they delegate responsibility.

The following procedures describe the Investigator responsibilities in the conduct of Research involving Human Participants.

12.2 **Definitions**

*Principal Investigator (“PI”):* is an individual who conducts Research or under whose immediate direction Research is conducted; or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team. While the FDA considers a PI and an Investigator to be synonymous, this document does not.

*Researcher:* is the PI and/or Investigator.

12.3 **Investigators**

12.3.1 **Principal Investigators**

Tulane ORA has adopted a policy entitled “Who Can Serve as A PI and Other Eligibility Requirements on Sponsored Projects” which sets forth the eligibility requirements and the duties and responsibilities of a Principal Investigator (“PI”) or Co-Principal Investigator (“Co-PI”) at the University. This Policy also describes the processes for requesting and approving exceptions to the PI eligibility requirements.

The IRB recognizes one PI for each study (although several Co-PIs may be included in addition to the PI). The PI has ultimate responsibility for the Research activities. This includes, among other things, ensuring that the trial is publicly registered before any subjects are enrolled in the study (see Section 18.6 for additional details). Additionally, PIs should refer to the Initial Submissions Checklist (TU Form 301) and Secondary Submissions Checklist (TU Form 302) to ensure that all submissions to the IRB are complete.

12.3.2 **Change in Principal Investigator**

If there is a change in the PI, the outgoing Investigator must submit an Application for Amendment (TU Form 601) to notify the IRB that he or she has relinquished the responsibilities of the PI to the person named, or will do so on a specific date. The newly named PI notifies the IRB that he or she has read the Protocol and agrees to accept the responsibilities of the PI.

12.3.3 **Student Investigators**

Students may not serve as PIs. They must have a faculty advisor who fulfills the PI eligibility criteria and who will serve as PI and faculty advisor on the study. If appropriate and the student obtains special permission from their Department Head and Dean of their school acknowledging their approval as a PI then consideration will be given by the IRB.
12.3.4 Research Team
The PI and other individuals, also known as key personnel, who contribute to the scientific development or execution of a project in a substantive, measurable way, whether or not they receive salaries or compensation under the Protocol.

12.4 Responsibilities
In order to satisfy the requirements of this policy, Investigators who conduct Research involving Human Subjects must:

1. Develop and conduct Research that is in accordance with the ethical principles in the Belmont Report
2. Develop a Research plan that is scientifically sound and minimizes risk to the subjects;
3. Have sufficient resources necessary to protect Human Subjects, including:
   - Access to a population that would allow recruitment of the required number of subjects.
   - Sufficient time to conduct and complete the Research.
   - Adequate numbers of qualified staff.
   - Adequate facilities.
   - A process to ensure that all persons assisting with the Research are adequately informed about the Protocol and their Research-Related duties and functions.
   - Availability of medical or psychological resources that subjects might require as a consequence of the Research.
4. Assure that all procedures in a study are performed with the appropriate level of supervision and only by individuals who are licensed or otherwise qualified to perform such under the laws of Louisiana and the policies of Tulane;
5. Assure that all key personnel are educated in the regulatory requirements regarding the conduct of Research and the ethical principals upon which they are based;
6. Protect the rights and welfare of prospective subjects;
7. Ensure that risks to subjects are minimized: (i) By using procedures which are consistent with sound Research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes
8. Recruit subjects in a fair and equitable manner
9. Obtain and document informed consent as required by the IRB and ensuring that no Human Subject is involved in the Research prior to obtaining their consent;
10. Have plans to monitor the data collected for the safety of Research subjects;
11. Protect the Privacy of subjects and maintain the Confidentiality of data;
12. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as Children, Prisoners, Pregnant Women, mentally disabled persons, or
15. Have a procedure to receive complaints or requests for additional information from subjects and respond appropriately;
16. Ensure that pertinent laws, regulations, and Institution procedures and guidelines are observed by participating Investigators and Research staff;
17. Ensure that all Research that qualified as Human Subjects receives IRB review and approval in writing before commencement of the Research;
18. Comply with all IRB decisions, conditions, and requirements;
19. Ensure that Protocols receive timely continuing IRB review and approval;
20. Report Unanticipated Problems involving risk to subjects or other or any other reportable events to the IRB (see Section 9);
21. Obtain IRB review and approval in writing before changes are made to approved Protocols or consent forms;
22. Seek IRB assistance when in doubt about whether proposed Research requires IRB review; and
23. If the Research is subject to the ICH-GCP Guidelines, refer to the HRPO policy entitled “International Conference on Harmonization (ICH) Good Clinical Practices (GCP), Applicability to Human Subjects Research.”

Investigators are encouraged to periodically complete the Investigator Self-Assessment Checklist (TU Form 201) to evaluate whether compliance with ongoing responsibilities is being met.

Regulations & Guidelines: FDA 21 CFR §312.53(c)(1); 21 CFR §312.60; 21 CFR §312.61; 21 CFR §312.62; 21 CFR §812.43(c)(4); 21 CFR §812.100; 21 CFR §812.140; AAHRPP III.1.B – G; III.2.C and D.

12.5 Training / Ongoing Education of Investigators and Research Team

As stated above, one component of a comprehensive HRPP is an education program for all individuals involved with Research subjects. Tulane is committed to providing training and an on-going educational process for Investigators and members of their Research team related to ethical concerns, Federal and State regulatory requirements and Tulane policies for the protection of Human Subjects. Research teams consist of anyone working directly with Human Subjects or with identifiable data or Biological specimens for Research Under the Auspices of the Institution. This includes investigators, Research nurses, coordinators, students, technicians working with identifiable data, and faculty advisors. It is the responsibility of the PI to ensure that the Research team in compliant with all initial and ongoing education as required by Tulane University polices and regulatory requirements.

This requirement is mandatory regardless of funding sources. The requirements also apply to Research that is considered Exempt from IRB review.
12.5.1 **Orientation**

All PIs and members of their Research team (also known as “key personnel”) must review core training documentation including:

- Tulane’s Standard Operating Policies and Procedures for Human Research Protection;
- The “Belmont Report: Ethical Principals and Guidelines for the Protection of Human Subjects of Research;
- Applicable Federal & State regulations

12.5.2 **Initial Education**

The PI, key Investigators, and all members of the Research staff must complete and submit the following prior to submitting Research Protocols for review and approval:

- Tulane requires CITI basic course in the Protection of Human Research Subjects;
- CITI course in Good Clinical Practice; and
- HIPAA Training

New Research Protocols and **Applications for Continuing Review** (TU Form 603) will not be accepted or receive final approval until all sub-Investigators and members of the Research team have completed the education requirements.

12.5.3 **Waiver of Initial Education**

If Investigators or members of their Research team have successfully completed Human Subject Research training equivalent to that required by the Institution within the last year, they may request a waiver of the requirement for Initial Education. However, all Investigators or members of their Research team must complete the requirements of Continuing Education.

12.5.4 **Continuing Education and Recertification**

All Investigators and members of their Research teams must meet Institution continuing education requirement every three (3) years after certification of initial education for as long as they are involved in Human Subject Research. There is no exception to this requirement. Acceptable refresher modules at the CITI web-based training site must be completed.

Investigators must submit evidence of continuing education prior to the expiration of their training certification. New Research Protocols and **Applications for Continuing Review** (TU Form 603) will not be accepted from PIs who have not submitted satisfactory evidence of continuing education.

Investigators who are also IRB Chair, IRB members, or HRPO staff will satisfy the training requirements for IRB members and staff described in this policy under Section 2.12.
12.5.5 Additional Resources

The HRPO will be available for scheduled in-services at departmental meetings. Also, human Research protection information will be made available on the HRPO Website at http://tulane.edu/asvpr/irb, with links to:

- Tulane policies and procedures
- Federal and State regulatory sites
- Newsletters
- Training opportunities

12.5.6 Investigator Concerns

Investigators who have concerns or suggestions regarding Tulane’s HRPP should convey them to the HRPO Director, IO, or University RCO or other responsible parties (e.g. college Dean, Departmental Chair, etc.) regarding the issue, when appropriate. The IO or HRPO Director will Research the issue, and when deemed necessary, convene the parties involved to form a response for the Investigator or make necessary procedural or policy modifications, as warranted. In addition, the IRB Chair and/or the HRPO Director will be available to address Investigators’ questions, concerns and suggestions.
13 Sponsored Research

13.1 Policy

Tulane’s ORA is responsible for ensuring that negotiations between Tulane and Sponsors relative to Clinical Investigations that will take place under the purview of Tulane’s IRB follow all relevant Federal and State laws, rules and regulations and Institutional policies and procedures.

The PI cannot commence research and/or otherwise enroll subjects until the IRB has approved the study and, to the extent that the activity is Sponsored, a fully executed sponsor agreement is in place between the Sponsor and the University.

Since TUHC serves as a primary site for Sponsored University Research, to the extent that Research under the purview of Tulane’s IRB takes place at TUHC, specific coordination takes place between Tulane, through ORA, and TUHC, consistent with a Master Clinical Trial Affiliation Agreement (“Master CTA Agreement”), which is intended to expedite collaborative Research between the two institutions. See ORA’s policy entitled Coordination of Clinical Trials between TU and TUHC for details.


13.2 Definitions

Self-Sponsored (or “Investigator-Initiated,” “Investigator-Sponsored,” or “Unsponsored”): refers to a situation in which the individual Investigator is a Tulane Investigator and is the holder of the IND or IDE and therefore assumes the duties of the Sponsor of the clinical Investigator under the applicable FDA regulations.

Sponsor (or “Sponsored”): is any person or party that provides funding to support the conduct of Research, usually through a specific statement of work and often with a related transfer of value to the Sponsor. A Sponsor does not actually conduct the investigation. A Sponsor can be governmental (e.g., Federal, State or a local government) or private (e.g., a company, individual donor or private foundation), as well as Self-Sponsored (e.g., where Institution is responsible for funding the involved activity). The funding mechanism may be through a grant, contract or cooperative agreement. [FDA 21 CFR §50.3; 21 CFR §56.102(j); 21 CFR §312.3(b)].

13.3 ORA Review

ORA is designated as institutional representative and is responsible for securing authorized signatures on awards with Sponsors. To this end, ORA serves as the intermediary between a Sponsor and the PI for purposes of negotiation, budget changes, modifications to an award, award date extensions, and other administrative matters. In consultation with the PI and/or Grants and Contracts Accounting, ORA reviews the award terms and conditions and the budget before obtaining authorized signatures. ORA and the PI are responsible for ensuring University compliance with the terms and conditions of the award, as well as any applicable Federal, State, and University regulations and guidelines.

For commercially sponsored clinical trials under the purview of Tulane’s IRB, when subject informed consent must be obtained, ORA will undertake the following:

1. The ORA Director (or delegate) will review sponsor agreements to ensure that they contain language reflecting:
a. Tulane’s commitment to the protection of human subjects involved in research;
b. That Tulane and sponsor will follow the protocol, applicable laws and regulations and ethical standards.
c. Identify who is responsible for payment with respect to research-related injuries.
d. Contain sponsor indemnification, as appropriate, for the research undertaken, for subject injury and use of research data and results.
e. Contain a summary of the study’s scope and a description of services to be provided by Tulane, if applicable Tulane University Hospital and Clinic, a study budget, and the reporting obligations of the parties.
f. If the sponsor discovers results that could affect the safety or medical care for the subjects, then the sponsor will make sure the IRB is notified.
g. If a study monitor is used to monitor the research and the study monitor uncovers information that could affect the safety of participants or their willingness to continue participation, influence the conduct of the study, or alter the IRB(s) approval to continue the study, then the sponsor will communicate such information to the IRB as soon as reasonably possible.
h. If the sponsor discovers results that could affect the safety or medical care for the subjects, then the sponsor will make sure the IRB is notified.
i. Notify Tulane’s HRPO that a fully executed sponsored agreement is in place between Tulane and the sponsor, which is a condition that must be met, in addition to IRB approval, before any subject enrollment can occur.

2. The ORA Director (or delegate) will review sponsored agreements and study information as necessary for each sponsored protocol to ensure that the informed consent and sponsored agreement language are consistent. To the extent that the informed consent is not consistent, ORA will highlight or bold the objectionable language (or make redline changes) to the informed consent and forward it to HRPO, which in turn communicates the inconsistencies to the PI. It is the ultimate responsibility of the PI to edit the informed consent and ensure that it is consistent with the sponsored agreement.

Upon request, ORA will furnish to the HRPO copies of sponsored research agreements involving clinical trials under the purview of Tulane’s IRB.

For additional details with respect to the Sponsored Research, refer to ORA’s policy entitled Submission and Routing of Proposals for Extramural Funding and Award Acceptance and the CTA Checklist used to coordinate review of sponsored agreements involving Human Subjects.
14 Conflicts of Interest in Research

14.1 Policy

Tulane policy and guidelines on conflict of interest (“COI”) include specific requirements applicable to COI associated with the conduct of Human Subjects’ Research Protocols. Matters involving COI, including Research COI, are governed by the Institution’s COI Policy (found at Part III.D.C of the Faculty Handbook entitled “Policy of Tulane University on Conflicts of Commitment and Interest for Investigators in Human Subjects Research”).

Pursuant to the University’s COI policy, Tulane maintains a Conflict of Interest Committee (“COI Committee”). Tulane’s IRBs will collaborate with the Tulane COI Committee to ensure that financial COI are identified and managed before Tulane’s IRB completes its review of any Protocol. This Section establishes procedures to implement this collaborative arrangement.

The IRB will determine:

- Whether the methods used for management of Financial Interests of individuals involved in the Research adequately protect the rights and welfare of Human Subjects;
- Whether other actions are necessary to minimize risks to Subjects; and
- The kind, amount, and level of detail of information that must be disclosed to Research Participants regarding:
  - The interests of individuals involved in performing the Research and
  - Any conflict management arrangements applied.

14.2 Definitions

Financial Interest: is (1) aggregate investments (whether in the form of debt, stock or other equity ownership, options or warrants to purchase stock or other securities or similar instruments) with a value exceeding $10,000 or representing a five (5%) percent or greater interest in any entity, enterprise or trust; (2) royalties on any patent or other intellectual property interests with a value exceeding $10,000, unless paid by Tulane; or (3) income, salary or remuneration in cash or in kind, emoluments, benefits, gifts, honoraria, travel expenses, goods or services with a value exceeding $10,000. Financial Interest does not include holdings in mutual funds or other equity funds in which the day-to-day control of investments is held by a person not subject to any Tulane COI policy. This definition is extracted from the Institution’s COI policy contained in the Faculty Handbook, Part III, D, Part A. The definition in the Faculty Handbook shall prevail to the extent that there is a conflict.

Research Financial Interest: is any investments (whether in the form of debt, stock or other equity ownership, options or warrants to purchase stock or other securities or similar instruments) or interest in a Sponsor, research or healthcare related organization; royalties on any patent or other intellectual property interests, unless paid by Tulane; or income, salary or remuneration in cash or in kind, emoluments, benefits, gifts, honoraria, travel expenses, goods or services received from a Sponsor or research or healthcare related organization. Research Financial Interest does not include holdings in mutual funds or other equity funds in which day-to-day control of investments is held by a person not subject to any Tulane University Conflict of Interest policy. Please note that Research Financial Interest has no dollar or ownership thresholds; therefore, any interest related to a Sponsor or to the research must be disclosed, however small. This definition is extracted from the Institution’s COI policy contained in the
Faculty Handbook, Part III, D, Part C. The definition in the Faculty Handbook shall prevail to the extent that there is a conflict.

14.3 Initial Review

In the initial IRB application for IRB approval of the Research Protocol, each Investigator must complete the COI section. To the extent that a potential financial COI exists involving a researcher or immediate family member in the Sponsor of the Research or in the results of the Research, then the Investigator must complete the Tulane Investigator Conflict of Interest Attestation Form (“Attestation Form”) that attests that he/she has supplied the COI Committee with a complete “Conflict of Commitment and Conflict of Interest Disclosure Form”, including “Form C: Annual Research-Related Financial and Leadership Disclosures” (hereinafter “Form C”) (and any required updates thereto). The Investigator also must indicate whether the Research he or she is conducting could be affected by any of his or her Research Financial Interests and/or “Leadership Roles” (found in the Faculty Handbook at Part III.A.e (definition section)). The IRB staff may not process applications for IRB approval and may not commence initial review of a Protocol until each Investigator has provided this required information (see Faculty Handbook, Part III.D.C.4).

If a potential protocol specific COI exists, then the Investigator must complete IRB Application (TU Form 102), Supplement N entitled “Research Involving Conflicts of Interest” which describes protocol-specific conflict information. The COI Committee will provide the IRB with a Disclosure Review form which summarizes the management plan approved by the COI Committee. In instances in which the COI Committee has not completed its review and conflict management plan, the IRB will defer initial Protocol review until the COI Committee review process is completed and the results made available to the IRB (see Faculty Handbook, Part III.D.C.4).

The IRB has final authority to determine whether the Research, the Financial Interest, and the management plan, if any, allow the Research to be approved. With regard to the conflict management plan issued by the COI Committee, the IRB shall either affirm or strengthen it. For example, the IRB can disagree with the COI Committee management plan and decide that the Research cannot go forward. Also, the IRB can include additional requirements to a proposed COI Committee management plan. However, the IRB cannot weaken a financial conflict of interest management plan proposed by the COI Committee.

The IRB shall notify the COI Committee, which in turn shall notify the PI of its findings and the approved management plan.

14.4 Continuing Review

At the time of Continuing Review of the Protocol, each Investigator must attest using the Attestation Form that he or she has supplied the COI Committee with a complete Conflict of Commitment and Conflict of Interest Disclosure Form, including Form C (and any required updates thereto), and must indicate whether the Research he/ she is conducting could be affected by any of his or her Research Financial Interests and/or Leadership Roles. The IRB staff may not process Applications for Continuing Review (TU Form 603) for IRB approval and may not commence continuing review of a Protocol until each Investigator has provided this required
information. If, at the time for Continuing Review of a study, all necessary information has not been provided, the study shall not be authorized to continue and no new subjects shall be enrolled in the study unless the IRB determines that it is in the best interests of the previously enrolled subjects to continue the study and their participation.

Whenever a COI arises or is identified after IRB approval of Research, the Investigator will promptly disclose the conflict to the COI Committee and notify the IRB. The COI Committee will formulate a plan to manage the COI with respect to the Human Subjects’ Research activity and inform the IRB of its recommendations. The IRB or IRB Chair (or designee) will include the results of the COI Committee evaluation when it reviews an amendment involving a COI.

The IRB has final authority to determine whether the Research, the Financial Interest, and the management plan, if any, allow the Research to be approved. With regard to the conflict management plan issued by the COI Committee, the IRB shall either affirm or strengthen it. With respect to the Research, the IRB has final authority. For example, the IRB can disagree with the COI Committee management plan and decide that the Research cannot go forward. Also, the IRB can include additional requirements to a proposed COI Committee management plan. However, the IRB cannot weaken a financial conflict of interest management plan proposed by the COI Committee.

The IRB shall notify the Investigator of its findings and the approved management plan.

**14.5 Updated COIs and Failure of PIs to Complete Annual COI Form**

If at any time over the course of the year one or more Research Financial Interests or Leadership Roles of an Investigator or an “Investigator’s Immediate Family” (found in the Faculty Handbook at Part III.D.A.d (definitional section)) in any Research or health care-related organization changes in any material way, the Investigator must promptly notify the COI Committee of that change by submitting a written statement detailing such change(s) (Faculty Handbook, Part III.D.C.2). Investigators must also forward to the COI Committee without delay any amendments or changes that they make to any reports of Research Financial Interests that are submitted to any Sponsor of Research.

All Investigators must complete Form C of the Conflict of Interest and Conflict of Commitment Disclosure Form (found in the Faculty Handbook at Part III.D.C.2). This Form C must be submitted to the Investigator’s department Chair or Dean in accordance with Institutional policy and must be updated on an annual basis (by January 31 of each year) for as long as the Investigator continues to conduct any Research at the University.

Investigators must append to the Disclosure Form a copy of every report of their Research Financial Interests that they are required to submit to any Sponsor of Research. Any report of Research Financial Interests that is sent to a Sponsor of research anytime after the January 31 filing deadline must also be sent without delay to the COI Committee.

**14.6 IRB Review of COI**

The HRPO Director (or designee) will notify the Administrative Compliance Specialist for the University Conflict of Interest Committee (“COI Officer”) of any Protocol submissions involving disclosure of a potential COI. Where applicable, the COI Officer will inform the

---

12 This includes, but is not limited to, reports that must be made to Sponsors pursuant to regulations of the FDA.
individual of the procedures for disclosing a COI. The COI Officer will assure that all COI disclosures are reviewed in accordance with University policy, the Faculty Handbook, and Federal regulations. The COI Officer shall liaise with the HRPO Director and provide all required documents, including determinations by the COI Committee regarding its findings and management plans (as applicable), to the Convened IRB to assist it with its deliberations concerning potential protocol COIs.

In considering whether to affirm, strengthen the COI Committee’s management plan, the IRB should consider the following issues:

- Whether there is sufficient public disclosure of Financial Interests;
- Whether there is sufficient disclosure to subjects through the consenting process;
- Reduction of equity holdings;
- Divestiture of Financial Interest (complete or partial);
- Severance of relationships that create actual or potential COIs
- Clear separation of Research from paid activities;
- Disqualification of the Investigator with the conflict in obtaining consent and/or from participation in all or a portion of the Research; and
- More frequent continuing reviews by the IRB.

In considering whether a protocol specific COI exists, the IRB should consider the following additional issues with regard to the impact of the economic interests on:

- Study design;
- Protocol;
- Informed Consent document (particularly representations of risks and benefits);
- Data collection and reporting;
- Eligibility determinations and application of inclusion and exclusion criteria;
- Continuing consent
- Clinical determinations (e.g., dose modifications, removing patients from study, related care);
- Determination and reporting of unanticipated problems and their relationship with study mechanism for data and safety monitoring;
- Data made available on continuing review (i.e., integrity and sufficiency); and
- Consequences affecting the clinician researcher’s clinical duties to patient as a Participant.

With respect to protocol specific COIs, the IRB has the final authority to determine whether the interest and its management, if any, are sufficient for IRB approval. The IRB may disapprove Research that involves a COI or it may require changes at the Investigator’s or Sponsor’s expense to eliminate or manage the conflict. Possible IRB determinations include, but are not limited to:

- Requiring divestiture or termination of relevant economic interest;
- Requiring Investigator recusal from study;
• Altering participation by the Investigator in all, or a portion, of the Research funded;
• In case of equity, imposing a bar on insider trading, or requiring the transfer of securities to an independent financial manager or blind trust, or limiting the timing of sale or distributions;
• Monitoring of Research (i.e., independent review of data and other retrospective reviews for bias, objectivity, comprehensiveness of reporting);
• Requiring independent clinical review of appropriateness of clinical care given to Research Participants;
• Monitoring the consent process; and/or
• Requiring disclosure to institutional committees, Research Participants, journals and data safety monitoring boards.

The IRB has final authority to determine whether the Research, the Financial Interest, and the management plan, if any, allow the Research to be approved. With regard to the conflict management plan issued by the COI Committee, the IRB shall either affirm or strengthen it. With respect to the Research, the IRB has final authority. For example, the IRB can disagree with the COI Committee management plan and decide that the Research cannot go forward. Also, the IRB can include additional requirements to a proposed COI Committee management plan. However, the IRB cannot weaken a financial conflict of interest management plan proposed by the COI Committee.
15 Participant Outreach

15.1 Policy
Tulane is committed to ensuring that educational opportunities are offered to Research Participants, prospective Research Participants, and community members to enhance their understanding of Research involving Human Subjects at Tulane.

The following procedures describe how Tulane fulfills that responsibility.

Regulations & Guidelines: AAHRPP V.2.B.

15.2 Responsibility

It is the responsibility of the HRPO Director and the IRB Senior Program Coordinator to implement the procedures outlined below.

15.3 Outreach Resources and Educational Materials

The HRPO dedicates a section of its Website to Research Participants, which includes the following:

- Participants Bill of Rights;
- Frequently Asked Questions (FAQs);
- Tulane Participant brochures;
- Links to government Websites (e.g., OHRP, FDA, NIH, NCI); and
- Opportunity to submit community concerns, trial information, and receive feedback.

Tulane periodically provides in-services and presentations related to Research to community organizations to increase public awareness and educate potential Research Participants.

Regulations & Guidelines: AAHRPP V.2.A.

15.4 Questions, Concerns, and Complaints

All questions, concerns or complaints received by HRPO from any individual through the Concerns and Complaint Form (TU Form 604) or any form of communication (i.e., written, verbal, or electronic) will be promptly acknowledged and forwarded to the appropriate individual within the Institution for handling and follow-up.

The time frame for resolution of complaints is dependent upon the nature and complexity of the issue.

HRPO contact information for reporting concerns or complaints will be provided in the Informed Consent Document, Participant Brochure and the HRPO Website.

Regulations & Guidelines: DHHS 45 CFR §46.116(a)(6)-(7); FDA 21 CFR §50.25(a)(6)-(7); FDA Information Sheets: A Guide to Informed Consent; AAHRPP V.1.B.

15.5 Evaluation

Tulane periodically evaluates its outreach activities and makes changes when appropriate. These evaluations take place in an informal, ongoing manner. All HRPO staff, IRB members, IRB Chairs and IRB Vice-Chairs will report both positive and negative feedback about all HRPO
outreach activities to the HRPO Director who will then track the input and any changes made to
improve outreach activities. The HRPO Director will summarize the material annually. In order
to formally evaluate its outreach activities, the HRPO Director and IRB Senior Program
Coordinator will determine:

1. The specific community outreach activities being used; and
2. Whether or not these community outreach activities have an evaluative component, and if
   so what, if any, changes in the outreach activities have resulted from these Evaluations.

The HRPO Director and IRB Senior Program Coordinator will administer surveys annually to
determine the adequacy of outreach activities. The survey will assess:

1. The scope, the content and the adequacy of outreach activities and resources;
2. Whether the Research community is using the HRPO Website regarding Research
   participation;
3. Whether the Research community is using other educational materials to inform
   prospective Participants about their rights and welfare as Research Participants; and
4. Whether additional resources are needed to improve Participant outreach activities.

The results of the survey will be used to establish both the adequacy of current outreach activities
and any additional resources that may be needed to meet the needs of the Research community
regarding Participants outreach.
16 Health Insurance Portability and Accountability Act (HIPAA)

16.1 Historical Background

The Health Insurance Portability and Accountability Act of 1996, Public Law 104-91 ("HIPAA"), and DHHS regulations promulgated there under with respect to standards to protect PHI (the "HIPAA Privacy Rule"), impose obligations on the University to protect the privacy of and safeguard of such information. The HIPAA Privacy Rule went into effect on April 14, 2003. While the main impact of the HIPAA Privacy Rule is on the routine provision of and billing for health care, the Rule also affects the conduct and oversight of Research. Researchers, IRB staff and IRB members as well as Research administration must be aware of these requirements.

16.2 Health Care Component

Under the Privacy Rule, any entity that meets the definition of a Covered Entity, regardless of size or complexity, generally will be subject in its entirety to the Privacy Rule. However, the Privacy Rule provides a means by which many Covered Entities may avoid global application of the Rule, through the Hybrid Entity designation provisions. This designation will establish which parts of the entity must comply with the Privacy Rule.

Any single legal entity may elect to be a Hybrid Entity if it performs both covered and non-covered functions as part of its business operations. A covered function is any function the performance of which makes the performer a health plan, a health care provider, or a health care clearinghouse. To become a Hybrid Entity, the Covered Entity must designate the health care components ("Health Care Component") within its organization. Health Care Components must include any component that would meet the definition of Covered Entity if that component were a separate legal entity. A Health Care Component may also include any component that conducts covered functions (i.e., non-covered health care provider) or performs activities that would make the component a business associate of the entity if it were legally separate. Within a Hybrid Entity, most of the requirements of the Privacy Rule apply only to the Health Care Component(s), although the Covered Entity retains certain oversight, compliance, and enforcement obligations. Thus, Research components of a Hybrid Entity that function as health care providers and engage in standard electronic transactions must be included in the Hybrid Entity’s health care component(s), and be subject to the Privacy Rule. If such a Research laboratory is included in the Hybrid Entity’s health care component, then the employees or workforce members of the laboratory must comply with the Privacy Rule.

A Hybrid Entity is not permitted, however, to include in its Health Care Component, a Research component that does not function as a health care provider or does not conduct business associate-like functions. For example, a Research component that conducts purely research Research is not performing covered or business associate-like functions and, thus, cannot be included in the Hybrid Entity’s health care component.

The University intends to fully comply with its obligations under the HIPAA Privacy Rule. For this reason, Tulane has designated itself as a Hybrid Entity [see 45 C.F.R. 164.504(a), 164.504(b), and 164.504(c)] for HIPAA Privacy compliance purposes. [See Tulane policy entitled “Designation of Health Care Components and Hybrid Entities (GC-001)]. Furthermore, for HIPAA compliance purposes, the University has designated the following components ("Health Care Components") as being subject to the HIPAA Privacy Rule:
16.3 Policy

This policy pertains to the application of HIPAA Privacy to Research conducted under the Auspices of Tulane’s IRB. Do not confuse this with Tulane’s ongoing HIPAA Privacy program that applies to its Health Care Components (see Tulane’s Website at http://www.tulane.edu/~contract/HIPAA/ for related policies, procedures and forms).

PHI obtained by Tulane may not be Used internally or Disclosed to any outside person or organization for Research purposes without prior approval of the IRB. Tulane Researchers within the Health Care Component (i.e., TUMG) as designated by Tulane must abide by these SOPs with respect to HIPAA Privacy and all Institutional policies with respect to HIPAA Privacy and Security.

The following describe the procedures for conducting Research at Tulane in accordance with the HIPAA Privacy Regulations.

16.4 Definitions

Authorization (or “HIPAA Authorization”): for HIPAA purposes, is a written document completed and signed by the individual that allows use and Disclosure of PHI for specified purposes, which are generally other than treatment, payment, or health care operations of a Covered Entity. [45 CFR §164.501 and §164.508].

Coded: means (1) Individually Identifiable Private Information (e.g., name or social security number) that would enable the Investigator to readily ascertain the identity of the individual to whom the Private Information (or specimens) pertains has been replaced with a number, letter, symbol, or combination thereof (i.e., the Code); and (2) a key to decipher the Code exists, enabling linkage of the Individually Identifiable Private Information (or specimens).

Covered Entity: for HIPAA Privacy purposes, is the term applied to institutions that must comply with the HIPAA Privacy and Security Rule. They include: health plans, health care clearinghouses; and health care providers. [DHHS 45 CFR §160.103; 45 CFR §164.504]. See Section 16.4 for details.

De-Identified Information: for HIPAA Privacy purposes, Health Information that does not identify an individual and with respect to which there is no reasonable basis to believe that the information can be used to identify an individual. If information is de-identified, it no longer is subject to the Privacy Rule and exempt from HIPAA. [45 CFR §164.514(a) and (b); 45 CFR §164.502(d)(permitted uses and Disclosures of De-Identified Information)].

Disclosure (or “Disclosure of PHI”): for HIPAA Privacy purposes, a Disclosure is the release, transfer, provision of access to, or divulging in any other manner IIHI outside of the Covered Entity. [45 CFR §164.501].
**Health Information:** for HIPAA Privacy purposes, it means any information, whether oral or recorded in any form or medium, that: (1) is created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university, or health care clearinghouse; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual. [DHHS 45 CFR §160.103].

**Hybrid Entity:** for HIPAA Privacy purposes, it is a single legal entity that (a) is a Covered Entity; (b) whose business activities include activities covered and not covered under the HIPAA Privacy Regulations; and (c) that designates health care components that will be subject to HIPAA. [45 CFR §164.103.]

**Individually Identifiable Health Information ("IIHI"):** for HIPAA Privacy purposes, this is information, including demographic information collected from an individual, that: (i) is created or received by a health care provider, health plan, employer, or health care clearinghouse; (ii) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual; and (iii) identifies the individual; or with respect to which there is a reasonable basis to believe the information can be used to identify the individual. [45 CFR §160.103]. This term should not be confused with “Individually Identifiable Private Information,” which is not covered by HIPAA.

**Limited Data Set:** for HIPAA Privacy purposes, is PHI that excludes specific direct identifiers of the individual or of relatives, employees or household members of an individual. A limited data set can only be used for the purposes of research, public health, or healthcare operations, and disclosed for the purpose of research.

**Minimum Necessary:** for HIPAA Privacy purposes, this refers to the principle that any access (i.e., obtaining or using PHI by any means or in any medium) to PHI by Tulane workforce members should be limited to the minimum amount of PHI needed to accomplish the intended purpose of the use or Disclosure. [DHHS 45 CFR §164.502(b) and §.514(d)].

**Preparatory Research:** for HIPAA Privacy purposes, Preparatory Research is the method applied to developing or designing a research study. [45 CFR §164.512(i)(1)(ii)].

**Protected Health Information ("PHI"):** for HIPAA Privacy purposes, PHI means IIHI that is transmitted or maintained in any form or medium (i.e., electronic, paper or verbal). [45 CFR §164.501]. PHI does not include IIHI in:

- Education records covered by the Family Educational Right and Privacy Act, as amended, 20 U.S.C. 1232g;
- Records described at 20 U.S.C. 1232g(a)(4)(B)(iv); and
- Employment records held by a covered entity in its role as an employer.

**Privacy:** for Research purposes, having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. Do not confuse this Research term with HIPAA Privacy requirements.

**Privacy Board:** for HIPAA Privacy purposes, Privacy Board is the term used to describe a board comprised of members of varying backgrounds and appropriate professional competencies, as
necessary, to review individual’s private rights. It is an alternative to an IRB for privacy issues only. It cannot replace the IRB for Common Rule or FDA purposes. Tulane’s IRB shall serve as the Privacy Board for the Institution.

Use: means, with respect to IIHI, the sharing, employment, application, utilization, examination, or analysis of such information within the organization that maintains such information. [45 CFR §164.501].

Waiver of Authorization (or “Waiver of HIPAA Authorization”): For HIPAA Privacy purposes, this is a means of requesting approval from an IRB or Privacy Board rather than asking each Research subject for an Authorization to access PHI. [45 CFR §164.512(i)(1)(i)].

16.5 Effects of HIPAA on Research

Before the Privacy Rule, protection of Human Subjects in Research focused primarily on assuring that the Research project was performed ethically and that the Human Subjects participated on the basis of informed consent. Federally Sponsored research is generally subject to the requirements of the Common Rule. This is the set of standards common to Federal agencies funding Research involving Human Subjects. It attempts to minimize the risk to which the subjects are exposed and assures continuing oversight by IRBs. While the Common Rule acknowledges the importance of Confidentiality, it does not have extensive requirements regarding the matter. Likewise, the FDA regulations governing clinical trials of new drugs and medical devices have some restrictions protecting the Confidentiality of Human Subjects. The Privacy Rule does not make any changes to these Research requirements. The HIPAA Privacy Rule supplements Research regulations within Tulane’s Health Care Component (i.e., TUMG); it does not replace them.

The Privacy Rule also contains several provisions that resemble Federal Research provisions and does make reference to those provisions. For example, the Common Rule contains specific requirements for a composition of an IRB. Similarly, the Privacy Rule contains specific requirements for a Privacy Board. The composition of a Privacy Board is similar to that of an IRB and, effectively, the IRB can easily serve as the Privacy Board for a Covered Entity.

The HIPAA Privacy Rule includes a number of important requirements that apply to Research. Helpful resources for more information on how HIPAA applies to Research can be found at:

- “NIH HIPAA Privacy Rule Booklet for Research” [see http://privacyruleandresearch.nih.gov];
- The “NIH Fact Sheet on IRB and HIPAA” [see http://privacyruleandresearch.nih.gov/pdf/IRB_Factsheet.pdf]; and
- “Impact of the Privacy Rule on Academic Research,” a white paper published by the American Council on Education [see http://acenet.edu/AM/Template.cfm].

16.6 Privacy Board

Tulane designates its IRB as its Privacy Board for purposes of Institutional determinations of whether PHI created, maintained or stored as a result of Human Subject Research can be Used or Disclosed without subject authorization or pursuant to an alteration of subject authorization. Tulane’s Privacy Board shall be established and operated consistent with 45 CFR §164.512(i) of the Privacy Rule, which states that:
• Members must have varying backgrounds and appropriate professional competencies as necessary to review the effect of the Research Protocol on individuals’ privacy rights and related interests;

• Each Board must have at least one member who is not affiliated with the Covered Entity or with any entity conducting or Sponsoring the Research and who is not related to any person who is affiliated with such entities; and

• Members may not have COI regarding the projects they review.

Do not confuse Tulane’s Privacy Board with its Privacy Official. The role of the Privacy Board is solely to determine whether PHI related to Human Subject Research can be Used or Disclosed without subject authorization or pursuant to an alteration of subject authorization. The Privacy Officer is responsible for overseeing and implementing all other HIPAA Privacy compliance requirements for the Institution with respect to TUMG, its participating physicians and clinicians, and all University employees and business units who provide management, administrative, financial, legal, and operational support to or on behalf of TUMG and have been designated as part of the University’s Health Care Component. [see Tulane policy entitled “Privacy Official,” (GC-019)].

Tulane University Hospital and Clinic (“TUHC”) is a separate legal entity from the University, with separate control and operation. It is a Covered Entity for HIPAA Privacy compliance purposes and has its own policies and procedures to ensure compliance with the Privacy Regulations. Tulane’s IRB does not serve as a privacy board or privacy officer for TUHC.

16.7 Permitted Uses and Disclosures of Research PHI

The Privacy Rule permits Covered Entities to Use or Disclose PHI for Research purposes when the individual who is the subject of the information authorizes the Use or Disclosure. For clinical trials, a HIPAA Authorization must be sought in addition to informed consent. The HIPAA Authorization also must be sought for other Research Uses or Disclosures of PHI that do not qualify for an IRB Waiver of Authorization (discussed below).

The Privacy Rule has several special provisions that apply to Research Authorizations for Uses and Disclosures of PHI for Research purposes. These requirements for Tulane with respect to Tulane’s Health Care Component (i.e., TUMG) are as follows:

1. An HIPAA Authorization purpose may state that the Authorization does not expire, that there is no expiration date or event, or that the Authorization continues until the end of the Research study; and

2. HIPAA Authorization Forms must be filled out completely and accurately by the Investigator, to ensure that all parties who require access to PHI for the Research (including Sponsors, CROs, DSMBs, IRBs, etc.) are identified in the form and may receive the information. The Authorization Form should be completed by the Investigator and submitted to the Tulane IRB for review and approval.

At Tulane, the HIPAA Authorization Form for the Use or Disclosure of PHI must be a separate document from the Informed Consent Form.
16.8 Research under HIPAA

HIPAA defines Research as "a systematic investigation, including Research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge." [45 CFR §164.501]. This definition is identical with the one used in the Common Rule, separate Federal legislation designed to protect Human Subjects involved in Research. HIPAA describes Privacy standards for protecting PHI and so only applies to Research that involves Humans Subject (not animals) health information.

16.8.1 Waiver of Authorization for Use or Disclosure of PHI in Research

16.8.1.1 Background

Under the Privacy Rule, covered entities are permitted to Use and Disclose PHI for Research with individual Authorization, or without individual Authorization under limited circumstances. A Covered Entity (or with respect to Tulane, its Health Care Component (i.e., TUMG)) may Use or Disclose PHI for Research when presented with documentation that an IRB has granted a Waiver of Authorization. [See 45 CFR §164.512(i)(1)(i)]. This provision of the Privacy Rule might be used, for example, to conduct records Research, epidemiological studies, or other Research where de-identified data is unavailable or not suited to the Research purpose.

16.8.1.2 Procedure for Uses & Disclosures Without an Authorization:

Unless an exception exists below (see Sections “a,” “b” and “c” below), the Institution must obtain individual HIPAA Authorization to Use and/or Disclose PHI for Research purposes. This HIPAA Authorization must contain the core elements required for all HIPAA Authorizations.

a. Uses and Disclosures of Research PHI Without an Authorization: The Health Care Component of Tulane may Use and/or Disclose PHI for Research without obtaining a HIPAA Authorization provided that it has obtained the following:

- Representations from the Researcher that the use and/or disclosure is sought solely to prepare for research, no PHI will be removed from the Organization, and the PHI sought is necessary for the research (see the Form entitled “Researcher Certification Regarding the Use and Disclosure of Health Information for Research Purposes”);
- To the extent that research pertains to a deceased patient, representations from the researcher that the PHI in fact belongs to a decedent, that the use or disclosure is solely for research, documentation of the patient’s death, and that the PHI is necessary for research (see the Form entitled “Researcher Certification Regarding the Use and Disclosure of Health Information for Research Purposes”); and
- Approval of an alteration or waiver of the HIPAA Authorization (in whole or in part) by Tulane’s IRB (acting in the capacity as a Privacy Board) (see the Form entitled “IRB Certification of Waiver/Alteration of Patient Authorization for Research Purposes”).

b. Uses and Disclosures of Research PHI Under Waiver/Alteration of HIPAA Authorization: To Use and/or Disclose PHI under a waiver/alteration by Tulane’s IRB (acting as the Privacy Board), certain statements must be documented. (See Section “a” above with respect to “IRB Certification of Waiver/Alteration of Patient
Authorization for Research"; and “Researcher Certification”. The following items must be included in the documentation:

- A statement identifying Tulane’s IRB (acting as the Privacy Board) and the date on which the waiver/alteration was approved;
- Specific waiver criteria, which are more fully discussed in Section “c” below;
- A brief description of the PHI necessary for Research to be conducted;
- A statement that the waiver/alteration has been reviewed and approved by the Tulane’s IRB (acting as the Privacy Board); and
- Evidence that the documentation of the waiver/alteration has been signed by the IRB Chair (or designee).

c. Waiver/Alteration Criteria: Documentation must exist that contain IRB/Privacy Board assurances that the waiver/alteration of the HIPAA Authorization meets certain criteria, including:

- The Use or Disclosure of PHI involves no more than a minimal risk to a subject’s privacy, based on an adequate plan to protect identifiers from improper Use and Disclosure, an adequate plan to destroy identifiers at the earliest opportunity consistent with the research and absent a health or Research justification for retaining that information, and adequate written assurances by the PI that the PHI will not be re-Used or Disclosed to anyone else, except as is required by law, for oversight of the research itself, or for other permitted research;
- The Research could not practicably be conducted without the waiver/alteration; and
- The Research could not practicably be conducted without access to the PHI.

d. Effect of Prior Authorizations: HIPAA Authorizations obtained prior to April 14, 2003 will continue to be valid unless a specific expiration date is noted in the HIPAA Authorization. Without an expiration date, the Institution may continue to use and disclose that PHI for Research purposes in perpetuity.

e. Retention Requirements: The Institution must maintain documentation of the IRB’s (acting as a Privacy Board) approval of the waiver/alteration of the HIPAA Authorization for at least six (6) years from the date the waiver/alteration was obtained.

16.8.2  Review Preparatory to Research

The Privacy Rule permits a Covered Entity to Use or Disclose PHI to a Researcher without Authorization or Waiver of Authorization for the limited purpose of a “review preparatory to research.” [45 CFR §164.512(i)(1)(ii)]. Such reviews may be used to prepare a Research Protocol, or to determine whether a Research site has a sufficient population of potential Research subjects. Prior to permitting the Researcher to access the PHI, the Covered Entity must obtain representations from the Researcher that the Use or Disclosure of the PHI is solely to prepare a Research Protocol or for similar purposes preparatory to Research, that the Researcher will not remove any PHI from Tulane, and that PHI for which access is sought is necessary for the Research purpose. Researchers should consult the Covered Entity regarding any forms or applications necessary to conduct a review preparatory to Research.
Researchers conducting a review preparatory to Research may not record information in identifiable form, nor may they Use the information that they receive to contact potential subjects. Because the Privacy Rule permits a Covered Entity to disclose PHI to the individual who is the subject of the information, covered health care providers and patients may continue to discuss the option of enrolling in a clinical trial without patient Authorization. Even when permitted by the Privacy Rule, however, any Use of patient information for recruitment must comply with IRB recruitment policies.

1. All Human Subjects Research requires IRB review to determine either a) Exempt status or b) need for further review.

2. Reviews preparatory to Research that are permitted under HIPAA may or may not be Human Subjects Research depending on the investigation being conducted.

- Only those reviews of a database by an individual entitled to access that database intended to enumerate an available data set without reviewing PHI and for which no PHI is recorded do not require review. For example: medical records may be queried for information such as: In the year XXXX how many patients had a discharge diagnosis of [indicate disease/diagnosis]. IRB Privacy Board Review is required for all other Uses of PHI as indicated.

- If the Research involves a de-identified data set, defined as removing the following identifiers, then a de-identified data set certification form must be completed submitted for administrative review and certified prior to accessing the data set. This activity also requires an IRB determined Exemption from review:
  i. Names
  ii. Geographic info. (city, state, and zip)
  iii. Elements of Dates (except years)
  iv. Telephone numbers
  v. Fax numbers
  vi. E-mail address
  vii. Social Security numbers
  viii. Medical Record, prescription numbers
  ix. Health Plan Beneficiary numbers
  x. Account numbers
  xi. Certificate /License numbers
  xii. VIN and Serial #s, license plate numbers
  xiii. Device identifiers, serial numbers
  xiv. Web URLs
  xv. IP address numbers
  xvi. Biometric identifiers (finger prints)
xvii. Full face, comparable photo images
xviii. Unique identifying numbers

IRB Privacy Board review and approval is required prior to initiating this Research. Investigators are not authorized to contact potential Research subjects identified in reviews preparatory to Research.

16.8.3 Research on PHI of Decedents

The protections of the Common Rule apply to living human beings. By contrast, the Privacy Rule also protects the PHI of deceased persons (“Decedents”). [see 45 CFR §164.512(f)(4)]. The Privacy Rule contains an exception to the Authorization requirement for Research that involves the PHI of Decedents. A Covered Entity may Use or Disclose Decedents’ PHI for Research if the entity obtains representations from the PI that the Use or Disclosure being sought is solely for Research on the PHI of Decedents, that the PHI being sought is necessary for the Research, and, at the request of the Covered Entity, documentation of the death of the individuals about whom information is being sought. (see the Form entitled “Researcher Certification Regarding the Use and Disclosure of Health Information for Research Purposes”). Researchers should submit the applicable IRB form for IRB approval when they intend to conduct Research involving Decedents’ PHI. The IRB (acting as the Privacy Board) must then document its approval of an alteration or waiver of the HIPAA Authorization (in whole or in part) by Tulane’s IRB (see the Form entitled “IRB Certification of Waiver/Alteration of Patient Authorization for Research Purposes”).

16.8.4 Limited Data Sets with a Data Use Agreement

When a Researcher does not need direct identifiers for a study but does require certain data elements that are not permitted in de-identified data, the Privacy Rule permits a Covered Entity to Disclose a Limited Data Set to the Researcher without Authorization or Waiver of Authorization, provided that the Researcher has signed a data use agreement. [See 45 CFR §164.514(e)(1)]. The Limited Data Set is still considered to be PHI, but it must exclude only specified direct identifiers of the individual or of relatives, employers, or household members of the individual.

A Limited Data Set is defined as removing the following 16 identifiers:

1. Names
2. Postal address info. (if other than city, state and zip)
3. Telephone and fax numbers
4. E-mail addresses
5. Social Security numbers
6. Medical record, prescription numbers
7. Health plan beneficiary numbers
8. Account numbers
9. Certificate/license numbers
10. Vin and serial numbers
11. license plate numbers
12. Device identifiers
13. Serial numbers
14. Web URLs
15. IP address numbers
16. Biometric identifiers (finger prints)
17. Full face, comparable photo images

The Privacy Rule requires that the data use agreement used in conjunction with the Limited Data Set contain provisions that:

1. Establish the permitted Uses and Disclosures of the Limited Data Set by the recipient, consistent with the purposes of the Research, and which may not include any Use or Disclosure that would violate the Rule if done by the Covered Entity;

2. Limit who can Use or receive the data; and

3. Require the recipient to agree to the following:

4. Not to Use or Disclose the information other than as permitted by the data use agreement or as otherwise required by law;

5. Use appropriate safeguards to prevent the Use or Disclosure of the information other than as provided for in the data use agreement;

6. Report to the Covered Entity any Use or Disclosure of the information not provided for by the data use agreement of which the recipient becomes aware; Ensure that any agents, including a subcontractor, to whom the recipient provides the Limited Data Set agrees to the same restrictions and conditions that apply to the recipient with respect to the Limited Data Set; and

7. Not to identify the information or contact the individual.

8. Researchers who will be receiving Limited Data Sets must submit a signed copy of the Covered Entity’s data use agreement to the Tulane IRB for approval, prior to initiating the Research. Transition Provisions

The Privacy Rule contains certain grandfathering provisions that permit a Covered Entity to Use and Disclose PHI for Research after the Rule’s compliance date of April 14, 2003, if the Researcher obtained any one of the following prior to the compliance date:

1. An Authorization or other express legal permission from an individual to Use or Disclose PHI for the Research;

2. The informed consent of the individual to participate in the Research; or

3. An IRB waiver of informed consent for the Research.
16.9 Transition Provisions:
The Privacy Rule contains certain grandfathering provisions that permit a Covered Entity to Use and Disclose PHI for Research after the Rule’s compliance date of April 14, 2003. [45 CFR §164.532]. If the Researcher obtained any one of the following prior to the compliance date:

1. An Authorization or other express legal permission from an individual to Use or Disclose PHI for the Research;
2. The informed consent of the individual to participate in the Research; or
3. An IRB waiver of informed consent for the Research.

Even if informed consent or other express legal permission was obtained prior to the compliance date, if new subjects are enrolled or existing subjects are re-consented after the compliance date, the Covered Entity must obtain the individual’s Authorization. For example, if there was a temporary waiver of informed consent for emergency Research under the FDA’s Human Subject protection regulations, and informed consent was later sought after the compliance date, individual Authorization must be sought at the same time.

The transition provisions apply to both Uses and Disclosures of PHI for specific Research Protocols and Uses or Disclosures to databases or repositories maintained for future Research.

16.10 HIPAA and Documentation Requirements
HIPAA documents include a HIPAA Authorization Form, a Waiver of HIPAA Authorization Form, and a De-Identification Form. One of these documents must be used whenever PHI is utilized in the Research.

16.11 Patient Rights and Research
Under HIPAA, patients have certain rights. Those that may affect Research include the right to receive a Notice of Privacy Practices, the right to access, inspect, and receive a copy of one’s own PHI, the right to request an amendment to one’s own PHI, and the right to an accounting of certain Disclosures of PHI that occur outside the scope of treatment, payment and health care operations that have not been authorized.

16.12 HIPAA and Existing Studies
Any Research subject enrolled in a study that Uses PHI from a Covered Entity must sign a HIPAA-compliant HIPAA Authorization Form. This form is in addition to the existing Informed Consent document, and is Federally required. The Tulane HIPAA Authorization Form may be located on the Tulane HRPO Website: http://tulane.edu/asvpr/irb.
17 Collaborative Research and Off-Site Research

17.1 Background

Researchers at Tulane frequently interact with entities or individuals outside the Institution in furtherance of their Human Subjects Research. The University (and its Researchers) regulatory obligations and alternatives for addressing them differ depending on the relationship with the entity or individual outside the University in the context of the Research project. In analyzing the many types of relationships that exist between the University and its Researchers, on one hand, and outside entities and individuals, on the other, a primary distinction is between those that are “engaged” in the Human Subjects Research versus those that are not engaged. This distinction is important because each engaged institution is responsible for safeguarding the rights and welfare of Human Subjects and for complying with applicable laws and regulations (including the Common Rule, as appropriate) and with its own human research protection program policies and procedures.

This policy ensures that the University can fulfill its affirmative obligation to assure appropriate oversight of Research in which the University is “engaged” and also, under certain circumstances, of other “engaged” entities associated with University Research. This policy also describes the process for coordination of IRB Research review and oversight for Tulane Research involving Human Subjects which is conducted at off-site locations or at multiple sites.

17.2 Policy

Off-Site Research is subject to special procedures for coordination of Research review and may involve more than one IRB responsible for Research oversight. In these cases, Tulane has established additional procedures to define the responsibilities of each IRB, coordinate communication among responsible IRB committees, and manage information obtained in off-site or multi-site research to ensure protection of Human Subjects. In coordinating Off-Site Research reviews, the VPR, in consultation with HRPO and Tulane Office of General Counsel, takes into consideration the source of funding for the Research activity, Federal regulations, specific Sponsor regulations governing Human Subjects Research protections, and Institutional policy.

Tulane’s IRB requires additional information and documentation for Research that meets the definition of Off-Site Research. Institutional policies apply to all Off-Site Research involving Human Subjects regardless of funding source including all Un-sponsored Off-Site Research involving Human Subjects such as educational and other survey Research. HRPO staff are available to advise Investigators on meeting the specific Institutional and regulatory requirements for obtaining IRB approval of Off-Site Research.

In addition, Tulane may enter into formal agreements with other non-Tulane facilities to provide Research review (i.e., to act as the relied-upon IRB), to rely upon other institutions for Research review, or to cooperate in review. Tulane enters into these types of arrangements through a Memorandum of Understanding, IRB Authorization Agreement, or contract with the institution(s) in question.

17.3 Definitions

Cooperative Research: is defined as Research conducted in cooperation with and at a performance site of an institution or facility that is not owned or operated by Tulane or TUHC or
that does not fall under Tulane IRB’s authority. An Off-Site Institution or Off-Site Facility may be domestic or international and may or may not have its own IRB.

Engaged in Research: an institution is engaged in a Research project when its employees or Institutional Agents, for the purposes of the research project obtain: (1) data about the subjects of the Research through intervention or interaction with them; or (2) Individually Identifiable Private Information about the subjects of the Research or identifiable biological specimens; or (3) the informed consent of Human Subjects for the Research. Obtaining Individually Identifiable Private Information includes, but is not limited to: (1) observing or recording private behavior; (2) using, studying, or analyzing for Research purposes identifiable Private Information or identifiable specimens provided by another institution; and (3) using, studying, or analyzing for Research purposes Individually Identifiable Private Information or identifiable specimens already in the possession of the Investigators.

Off-Site Research (or “Non-Tulane Site,” “Off-Site Institution” or “Off-Site Facility” or “Off-Site Location”): is Human Subjects Research conducted under the auspices of Tulane’s IRB at performance sites that are not owned or operated by Tulane University or TUHC.

“On-Site Research” (or “Tulane Site”): is Human Subjects Research conducted under the auspices of Tulane’s IRB at performance sites that are owned or operated by Tulane University or TUHC.

17.4 Types of Collaborations

Tulane Researchers participate in a broad range of collaborative relationships with other Investigators and institutions. They include:

- **Tulane-affiliated institutions**—many Tulane investigators collaborate with Researchers at Tulane-affiliated entities, which includes any institution for which Tulane serves as the IRB-of-record (see OHRP’s Website at http://ohrp.cit.nih.gov/search/ for confirmation purposes);

- **Other U.S.-based academic institutions**—most if not all, academic institutions within the U.S., if they receive Federal funding, will have already obtained assurance of compliance through the FWA program. Investigators need to ensure that they or their collaborators meet the respective IRB-review requirements;

- **U.S.-based, non-academic hospitals, clinics, and practices**—Hospitals, clinics, and practices that are not affiliated with academic medical centers may not already have in place the IRB and FWA programs necessary for Federally-funded Research to take place. If Investigators are committed to working in these settings, they may be faced with finding a local IRB to review the study and with guiding the organization’s pursuit of assurance of compliance through the FWA program; and

- **International entities and Researchers**—Researchers who wish to conduct Human Subjects Research in countries outside the U.S. or its territories generally must obtain approval from the host country’s ethics committee and from Tulane’s IRB.

PIs should refer to the Coordination of IRB Research Review (TU Form 1004) found on HRPO’s Website for guidance with respect to the range of Research collaboration. As will be discussed below, these collaborations may vary widely in scope and complexity.
Sections 17.5 through 17.14 below summarize the range of options with respect to whether an Investigator or institution is engaged in Human Subjects Research and, if so, the appropriate assurance mechanism, required documentation and additional information requirements.

### 17.5 Research Involving Non-Tulane Performance Sites: Cooperative Research

1. The PI arranges for the Off-Site Facility administrator to submit a letter on the Off-Site Facility’s letterhead stationery addressing the following information:
   - Agreement of the Off-Site Facility’s administration for the Investigator to conduct the study at the particular Off-Site;
   - Review of the project by facility personnel with respect to issues of appropriateness for its Human Subjects population and adequacy to perform the Research procedures as approved by the Tulane IRB (i.e., the facility has the appropriate equipment and personnel to conduct the Research and/or store and dispense investigational drugs in a manner reviewed and approved by the Tulane IRB);
   - If applicable, assurance that personnel from the Off-Site Facility who collect data are responsible for implementing the Research following Tulane IRB-approved procedures. The facility administrator is responsible for including written confirmation that facility personnel have the appropriate expertise to carry out the research procedures as reviewed and approved by the Tulane IRB; and
   - If applicable, assurance that personnel from the Off-Site Facility who collect data have appropriate training in the protection of Human Subjects.

2. For Cooperative Research projects, the PI determines whether an Off-Site Facility is “engaged” in Research. An institution becomes "engaged" in particular non-exempt Human Subjects Research project when its employees or agents, for the purposes of the Research project, obtain either: (1) data about the subjects of the Research through intervention or interaction with them; (2) individually identifiable private information about the subjects of the Research; or (3) the informed consent of Human Subjects for the Research. [45 CFR §46.102(d),(f)]. An institution is automatically considered to be "engaged" in Human Subjects Research whenever it receives a direct DHHS award to support such Research. In such cases, the awardee institution bears ultimate responsibility for protecting Human Subjects under the award.

   The PI’s review should consider the nature of the involvement of off-site personnel in implementing Research procedures and/or collecting data at the site. OHRP has issued guidance (found at [http://www.hhs.gov/ohrp/humansubjects/guidance/engage08.html](http://www.hhs.gov/ohrp/humansubjects/guidance/engage08.html)) that PIs may find helpful. Upon request, HRPO staff will assist the PI in making determinations of whether the Off-Site Facility is engaged in Research.

3. When a performance site is not engaged in Research, it is the PI’s responsibility to assure the site’s facilities and resources are appropriate for the nature of the activities that will be conducted there. It also is the PI’s responsibility to notify the IRB promptly if a change in Research activities changes the performance site’s engagement in Research.

---

13 Agents include all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility.
4. If the Off-Site Facility is engaged in Research, the PI determines, with ORI assistance, whether the off-site facility requires an assurance mechanism. (See the Section 17.10).

5. A Cooperative Research site engaged in Research which has its own non-Tulane IRB is responsible for conducting the Research review for that site and providing the PI with appropriate documentation to submit to the Tulane IRB. This documentation includes the FWA number for all Federally funded Research and the non-Tulane IRB approval letter.

6. A Cooperative Research site that is engaged in Research and which does not have its own IRB may need to establish one (or contract with a “for-hire” IRB) prior to its participation in the Research. The cooperative site should register its IRB with the OHRP/FDA as instructed by those agencies, if appropriate.

7. **Coordinated or Joint IRB Review**: For Federally funded Research, an institution with an FWA that is participating in a cooperative project may enter into a joint review agreement, rely upon (or defer) to another qualified IRB, or make similar arrangements to coordinate the joint review. The University permits similar arrangements for non-Federally funded Research. In either case, the VPR (or designee) must approve the arrangement for either individual studies or categorically (e.g., facilitated review). Any coordinated or joint review effort requires a written agreement among the involved institutions, regardless of whether they maintain an FWA.

8. **Deferring to Tulane’s IRB**: 
   
a. In some cases, an Off-Site Facility may enter into an agreement with Tulane allowing the facility to rely on Tulane’s IRB to review, approve, and provide continuing oversight of the Off-Site Research. These circumstances may include but are not limited to the following: Research that is not greater than minimal risk; or Research involving non-Tulane institutions that do not have an IRB and are not the type of institution that would typically establish an IRB (e.g., a school system). Tulane may also serve as the relied-upon IRB if the PI of the study is a Tulane employee and he/she conducts the study at an Off-Site Facility. In such cases, the Off-site Facility may be asked to sign an **IRB Authorization Agreement** (TU Form 1002) (applicable to single projects), or **Individual Investigator Agreement** (TU Form 1003) to abide by the decisions and determinations of Tulane’s IRB in the conduct of the Research. (See the Section 17.11 below on Negotiation of IRB Authorization Agreements for Collaborating Institutions for details.)

   b. When Tulane’s IRB conducts research reviews for an Off-Site Facility, as appropriate to the agreement and in accordance with its standard policies and procedures for research review and oversight, the IRB ensures sufficient knowledge of local research context for the off-site location as detailed in Section 17.12 on **IRB Knowledge of the Local Research Context**.

   c. The IO, in consultation with the HRPO and, if appropriate, Tulane Office of General Counsel, makes the final determination whether Tulane’s IRB will serve as the relied-upon IRB for another institution. Approval of such requests should **not** focus solely on avoiding duplicative effort and review. Factors to consider include:

      - The time and resources required to accept the review, given the demands;
• The expertise required for initial and continuing review;
• The ability to comply with the requirements for “local” knowledge of the Research contact at the outside organization and any Research sites;
• The resources, ability, and willingness of the outside organization, the PI and the Research sites to handle complaints, review adverse events, and to monitor compliance with applicable laws and regulations and IRB requirements; and
• The ability and willingness to comply with any additional requirements the outside organization may impose on Tulane IRB’s review.

d. If authorized, documentation of deferred responsibility may take the form, as appropriate, of an IRB Authorization Agreement (TU Form 1002) (signed by Tulane’s IO and the appropriate representative of the other institution), a letter of cooperation from the non-Tulane facility administrator and/or an IRB approval from the non-Tulane IRB. The IO signs all agreements as the signatory official for Tulane under its FWA. Once signed, the Off-Site Facility’s FWA should be amended to reflect deferred responsibility to Tulane’s IRB.

e. The PI must coordinate with project personnel at the Off-Site Locations to initiate any required off-site research review.

f. Upon request, HRPO staff will assist the PI in identifying required documentation on a case-by-case basis and maintain copies of all documentation from each Off-Site Facility in the study file.

g. The PI submits documentation of approvals for Off-Site Research in the initial submission to Tulane’s IRB or as it becomes available and may authorize research to start at a site once Tulane IRB approves the Protocol. HRPO staff maintain this information in the HRPO database and the study files.

9. **Tulane Deferring to Another IRB:**

a. Under limited circumstances, Tulane also may agree to defer responsibility for IRB review to a non-Tulane institution’s IRB. However, even when Tulane defers to another institution to serve as the IRB-of-record, Tulane remains responsible for maintaining a system to protect Human Subjects involved in the Research. As the relying institution, Tulane continues to retain ultimate responsibility for safeguarding the rights and welfare of Human Subjects involved in Research at the performance site(s) and for educating members of its Research community to establish and maintain a culture of compliance with applicable laws and regulations with these SOPs and with Institutional policies relevant to protection of Human Subjects involved in Research. Tulane also remains responsible for implementing appropriate oversight mechanisms to ensure compliance with the determinations of the relying IRB.

b. For Tulane to defer responsibility, the non-Tulane IRB must have an approved FWA. Other criteria taken under consideration when determining whether or not Tulane will defer responsibility to another IRB include whether or not that institution is accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP), and/or whether the cooperating institution is willing to sign an agreement in which it assures Tulane that it complies with the same Federal regulations for the
protection of Human Subjects. Examples of circumstances in which Tulane may defer IRB review may include cases where: the funding agency requires it; the Tulane employee role is limited (e.g., data analysis only); the Research began at another institution prior to employment of the investigator at Tulane and remains active only at the other institution (and any funds supporting the Research remain under the control of the non-Tulane institution); and/or the Research is not greater than minimal risk. In cases where Tulane’s IRB relies on another non-Tulane IRB, the PI must ensure that Research activity does not begin prior to Tulane IRB review and approval of the documentation for each study site, as appropriate.

c. For less than minimal risk studies, the IO, the HRPO Director, or designee may make the final determination as to whether Tulane’s IRB will defer review and oversight responsibilities to another IRB. For greater than minimal risk studies, the IO, in consultation with the HRPO Director and, if appropriate, with Tulane’s Office of General Counsel, makes the final determination as to whether Tulane’s IRB will defer review and oversight responsibility to another IRB.

d. Documentation of deferred responsibility may take the form, as appropriate, of an IRB Authorization Agreement (TU Form 1002) (applicable to single projects), Individual Investigator Agreement (TU 1003) (applicable to single projects), a letter of cooperation from the non-Tulane facility administrator and/or an IRB approval from the non-Tulane IRB. The IO signs all agreements as the signatory official for Tulane under its FWA. Once signed, Tulane’s FWA should be amended to reflect the deferred responsibility.

e. The PI must coordinate with project personnel at the Off-Site Locations to initiate any required off-site research review.

f. Upon request, HRPO staff will assist the PI in identifying required documentation on a case-by-case basis and maintain copies of all documentation from each Off-Site Facility in the study file.

g. The PI submits documentation of approvals for Off-Site Research in the initial submission to Tulane’s IRB or as it becomes available and may authorize research to start at a site once Tulane IRB approves the Protocol. HRPO staff maintain this information in the HRPO database and the study files.

17.6 Research Projects Involving Multiple Sites Where Tulane is the Lead Site/Lead Investigator

1. Tulane’s default position on Research performed at multiple locations is that each must review and approve its own participation in the Research. Unless an exception is provided for in this policy, when the University is involved as the primary or coordinating Research center or the overall PI of Research conducted at multiple locations can serve as a PI (see Tulane policy entitled “Who Can Serve as a PI and Other Eligibility Requirements on Sponsored Projects”), the PI must assure Tulane’s IRB reviewing the Research that each performance location involved in the Research has been properly approved at that location before the Research is initiated there and must notify Tulane’s IRB if any lapse or other change in approval status occurs.
2. If Tulane is the lead site in a multi-site study or the Tulane Investigator is the lead Investigator, the PI provides additional information to Tulane’s IRB to ensure ongoing communication among the participating IRBs and sites. The Tulane Investigator submits the following information along with the IRB Application (TU Form 102):

- For each non-Tulane site, a contact name and contact information (e.g., phone or e-mail) and name of individual who is responsible for such contact;
- For each non-Tulane site, a letter from the appropriate administrator granting permission for the Investigator to conduct the Research at its site;
- For each non-Tulane site with an approved FWA, the non-Tulane site’s FWA number;
- For each non-Tulane site, the relied upon IRB and appropriate documentation as needed (if joint review, a copy of the non-Tulane site’s IRB approval letter).

3. Additionally, the Tulane investigator must submit to the IRB a written plan for the management of information that is relevant to the protection of human subjects, such as reporting unanticipated problems, Protocol modifications, and interim results from all participating sites.

4. Tulane does entertain requests to avoid duplicative reviews, although duplication of effort should not be the sole reason under which the University will agree to serve as the IRB-of-record for other engaged sites or to cede review of University Research to other IRBs (see Sections 17.11 through 17.13 below for details).

17.7 Research at Geographically Separate Off-Site Location with No Cooperating Institution/Facility/Organization

1. In the IRB Application (TU Form 102) the PI provides the necessary information, as appropriate, on the subject populations, the cultural context, and the languages understood by the Human Subjects.

2. If the IRB membership does not have the appropriate expertise to conduct the review, HRPO staff and/or the PI assists the IRB in identifying cultural consultants. The PI may supply the name of an appropriate consultant in the IRB application.

3. Cultural consultants may review consent forms, provide verifications of translations, and provide guidance on the impact of the Research on subjects and the impact of the culture on the Research to be conducted.

17.8 Research at Geographically Separate Tulane-Owned Site with Non-Tulane Employees

1. ORI staff assist the PI in determining whether the non-Tulane employees will actively participate in the implementation of Research procedures or will obtain individually identifiable private data about Human Subjects for Research purposes. If the non-Tulane employees are engaged in the Research, then the Tulane HRPP applies to those personnel. They must complete the appropriate Human Subjects protection training, and the PI lists them as study personnel in the IRB Application (TU Form 102).

2. The PI provides the IRB the necessary information, as appropriate, on the subject populations, the cultural context, and the languages understood by the Human Subjects.
3. If the IRB does not have the appropriate expertise to conduct the review, HRPO staff and/or the PI assists the IRB in identifying cultural consultants. The PI may supply the name of an appropriate consultant in the **IRB Application** (TU Form 102).

### 17.9 Sites Operating under a Formal Agreement with Tulane’s IRB

1. Tulane may enter into a formal agreement to serve as the relied-upon IRB for a single Off-Site Facility by signing a Memorandum of Understanding, contract, or other official written agreement. Unlike the **IRB Authorization Agreement** (TU Form 1002), which applies to single projects, a formal agreement provides for ongoing IRB oversight of some or all of the Research involving Human Subjects at the Off-Site Facility.

2. In these cases, the formal agreement outlines the relationship between the institutions and documents the authority granted to the institution to serve as the relied-upon IRB for the Off-Site Facility.

3. Sites operating under a formal agreement must file their own individual assurance with the OHRP and list the appropriate Tulane IRB committee(s) as the designated IRB on the assurance. The IO for Tulane and the authorized official for the Off-Site Facility sign all formal agreements.

4. The terms of the formal agreement specify appropriate Human Subjects education and training resources for Investigators at the cooperating site as well as education and training for Tulane IRB members pertaining to IRB knowledge of the local research context, including distinct subject populations (i.e., veterans, non-English speaking populations, etc.) See the Section 17.12 on **IRB Knowledge of Local Research Context** for additional details.

5. HRPO maintains a record of current formal agreements on file.

### 17.10 Negotiation of Federal Assurances for Collaborating Institutions (Applicable to Federally Funded Research)

1. The institution is responsible for ensuring that all performance sites and Investigators engaged in its Federally supported Research involving Human Subjects operate under an appropriate OHRP or other Federally approved assurance. In general, institutions affiliated solely through professional or collaborative arrangements apply to OHRP for their own assurance. OHRP offers a number of different assurance mechanisms, including the FWA, **Individual Investigator Agreement** (TU Form 1003) and **IRB Authorization Agreements** (TU Form 1002). If a Federal agency that is not a division of the DHHS supports the Research, there may be additional requirements. HRPO staff determine these additional requirements on a case-by-case basis with the Sponsoring agency.

2. Off-Site Facilities determine the appropriate assurance mechanism with assistance from the OHRP based on such issues as the funding source, nature of the research, ownership of the performance site, and affiliation of the individuals collecting the data.

3. The PI assists performance sites without an IRB which are “engaged” in research in obtaining the appropriate assurance and IRB approvals. The ORI advises the PI throughout the process, as appropriate.
4. Off-Site Facilities submit an application for an assurance to the OHRP and designate an institutional signatory official with authority to represent and commit the entire institution and all of its components to a legally binding agreement. If the signatory official is not legally authorized to represent an institution, it may not be covered under the assurance.

5. In some cases, an institution may operate under another institution’s assurance with the approval of the supporting agency. In such cases, Tulane may enter into a formal IRB Authorization Agreement (TU Form 1002) with the collaborating institution for review, approval, and continuing oversight of the research in question. (See Section 17.11 entitled Negotiation of an IRB Authorization Agreement with Collaborating Institutions for more information.)

6. The institution’s assurance may also cover independent investigators who are not an employee of the institution only in accordance with a formal written agreement of commitment to relevant Human Subject protection policies and IRB oversight. The institutions may formalize such agreements under an Individual Investigator Agreement (TU Form 1003) or by a commitment agreement developed by the institutions. The institution entering into the commitment agreement maintains the agreement on file and submits copies to OHRP upon request.

17.11 Negotiation of an IRB Authorization Agreement with Collaborating Institutions

1. Cooperative research studies involving multiple institutions may rely on cooperative review. In such cases, participating IRBs enter into a written cooperative review agreement identifying the specific IRB designated to provide review and detailing the respective responsibilities of the IRB and each institution under the review agreement.

2. Under an IRB Authorization Agreement (TU Form 1002) both institutions agree that one institution is responsible for providing IRB review and the second will rely on the other for IRB review for a single specified project. IRB Authorization Agreements (TU Form 1002) list the Federal assurance number for each institution, designate the specific project to which the agreement pertains, and specify that the agreement applies to no other research projects.

3. The authorized officials for both institutions must approve the agreement in writing. The IO signs all IRB Authorization Agreements (TU Form 1002) as the signatory official for Tulane under its FWA. Both institutions maintain an IRB Authorization Agreement on file and agree to submit the document to OHRP upon request.

4. The IRB which agrees to review studies conducted at another institution (i.e., the primary IRB) has the responsibility for initial and continuing review of the Research. The primary IRB takes into account the required criteria for approval, the applicable regulations (e.g. FDA 21 CRF 50 or 56), the facilities and capabilities of the other institution, the measures to be taken by the participating institution to ensure compliance with the IRB’s determinations, and community attitudes or local research context, as appropriate. (See the Section 17.12 on IRB Knowledge of Local Research Context for additional information.)

5. The primary IRB under an IRB Authorization Agreement (TU Form 1002) is responsible for conveying approvals to all participating sites, either directly to the IRB or through the respective PI.

6. In cases in which Tulane relies on another designated IRB under an IRB Authorization Agreement (TU Form 1002), the PI, with assistance from HRPO, is responsible for
providing information to the non-Tulane IRB assuring sufficient consideration of local research context for the Tulane component(s) of the study.

7. When Tulane’s IRB relies on a non-Tulane IRB for review of research under an IRB Authorization Agreement (TU Form 1002), it agrees to abide by the decisions and determinations made by the non-Tulane IRB.

8. Likewise, individual Investigators agree to abide by those same decisions and determinations and may not modify or alter the research Protocol without prior written approval of the non-Tulane IRB.

9. The PI sends all required reports directly to the non-Tulane IRB with copies to the Tulane IRB/HRPO, as appropriate.

17.12 IRB Knowledge of Local Research Context

1. In accordance with OHRP guidance, when Tulane IRB serves as the relied-upon IRB for another institution or when the Research involves distinct subject populations (non-English speaking populations, veterans, etc.), Tulane’s IRB must ensure that it possesses or obtains sufficient knowledge of the local research context even when the IRB is geographically removed from the off-site research location.

2. The PI supports the IRB in understanding the local research context by providing the IRB necessary information, as appropriate, on:
   - The anticipated scope of the Off-Site Facility’s research activities;
   - The types of subject populations likely to be involved;
   - The size and complexity of the institution;
   - Institutional commitments and regulations;
   - Applicable law;
   - Standards of professional conduct and practice;
   - Method for equitable selection of subjects;
   - Method for protection of privacy of subjects;
   - Method for maintenance of confidentiality of data;
   - Languages understood by prospective subjects;
   - Method for minimizing the possibility of coercion or undue influence in seeking consent;
   - Safeguards to protect the rights and welfare of vulnerable subjects.

3. In cases where Tulane’s IRB conducts non-local review, members must have sufficient knowledge of the community from which the subjects are drawn to ensure protection of subject rights and appropriateness of the consent process for the subject population. In addition, the IRB must be sensitive to community laws and mores. The IRB may ensure the necessary expertise and knowledge to make appropriate determinations regarding the local research context through one or more of the following activities, as appropriate to the level of risk and in accordance with OHRP guidance and FDA regulation:
• Personal knowledge of the local research context on the part of one or more IRB members, such knowledge obtained through extended direct experience with the research institution, its subject populations, and its surrounding community;
• Review of the proposed research by representatives from the facility or by one or more ad hoc or cultural consultants with knowledge of the local research context. Ad hoc or cultural consultants may provide comments or recommendations in writing to the IRB prior to the meeting or attend the convened meeting to participate in the review, either physically or through audiovisual or telephone conference, when participation is deemed warranted by the consultant(s) or any one member of the IRB;
• Systematic reciprocal documented interchange between the IRB and elements of the local research context through periodic visits to the research site by one or more IRB members/HRPO staff or University representatives in order to obtain and maintain knowledge of the local research context; periodic discussion with appropriate consultants knowledgeable about the local research context; interaction with one or more designated institutional liaisons; and/or review of relevant written materials;
• Appointment of an IRB member from the community in question.

4. The primary reviewer (or expedited reviewers) should identify the need for consultation with respect to local context considerations. Additionally, a request may be made to the IRB Chair to appoint a consultant in the following instances:

• By IRB members whenever the member determines the assigned Protocol requires expertise in a special area in which he/she is unable to review a Protocol adequately;
• By the IRB when it decides during its review that a consultant is needed to assist in the review of a Protocol; and/or
• By the IRB Chair

5. The IRB chair (or designee) shall assess whether the local context review is satisfied. See Section 2.9 for specifics with respect to use of consultants.

6. HRPO staff assist the PI in addressing the requirements for information on the local research context upon request.

7. HRPO staff assist the IRB in identifying appropriate consultants and distributing appropriate review materials pertaining to the local research context to IRB members, as appropriate.

8. HRPO staff maintain documentation in the database and the study file of the local research context and the measures taken to ensure sufficient IRB knowledge of that context.

7. The IRB includes the name and toll-free contact information for an HRPO contact in the consent document for non-local IRB review or designates an individual at the research site to serve as the contact to relay reports to the IRB.

8. In the minutes of the meeting or in the IRB file, HRPO staff or the IRB reviewer documents the procedures used to ensure that the IRB adequately considered community attitudes.
17.13 Responsibilities of Reviewing & Relying IRB & PI

Where one IRB relies on or defers responsibility for IRB review to another IRB, the following responsibilities exist:

17.13.1 Reviewing IRB

The reviewing IRB will:

- Conduct initial and continuing reviews, and will review amendments to approved Protocol and unanticipated problems or AEs that may arise, in accordance with all applicable Federal regulations.
- Have the authority to suspend the Research for failure to comply with conditions of approval or regulatory requirements.
- Notify the relying IRB of any unanticipated problems, suspensions or terminations of Research. The reviewing IRB will notify the Federal or funding agencies of these events consistent with their policies and procedures and cross copy the relying IRB on any such correspondence.
- Consider conflicts of interest and confirm, where appropriate, that the application or proposal for Human Subjects Research submitted to DHHS matches the Protocol submitted for IRB approval.
- Serve as the IRB of record.

17.13.2 Relying IRB

The relying IRB will rely on the IRB review of the reviewing IRB. It will not rereview the study. Another IRB may refuse, on a case-by-case basis, to rely on the review of the reviewing IRB.

17.13.3 PI Duties

1. **Investigators wishing to defer oversight to a non-Tulane IRB must:**
   - Provide a detailed written request to Tulane’s IRB describing the study and investigation and the basis in support of Tulane possibly deferring to another IRB.
   - Submit a Protocol package to the relying IRB that contains: A copy of the application submitted to the relying IRB, Protocol, notification letters, Unanticipated Problem Reports, amendments and all attachments to the application. A copy of the initial application must be furnished to Tulane’s IRB.

2. **When a Protocol has been Approved for Oversight by the Relying IRB, the PI must:** submit to the deferring IRB copies of the relying IRB’s approval letter as well as all forms approved by the relying IRB (e.g., Consent Form (TU Forms 402; 403; and 407), as well as a HIPAA Privacy section), and contact information for relying IRB staff.

3. **When a Protocol has been Approved for Oversight by Another IRB, the PI must:** Once the relying IRB is designated as the IRB-of-record for a study by Tulane, the PI’s interaction with the HRPO and Tulane’s IRB includes:
● Forward copies of all documents approved by the relying IRB, including approved consent forms, consent form revisions, approved changes to the local consent/permission/assent form,

● Continuing Reviews: Continuing Review will be conducted by the relying IRB. Copies of all applicable paperwork submitted to the relying IRB should also be sent to Tulane’s IRB, along with a copy of relying IRB’s review for the study, the updated local consent form, and Tulane’s Application for Continuing Review (TU Form 603). Materials will be reviewed and consents will receive updated stamping by HRPO Director (or designee).

● Unanticipated Problems must be submitted to the HRPO for all subjects enrolled through Tulane, in accordance with IRB policy.

● Any local personnel changes, local advertisements etc. must be submitted to the HRPO for review and approval. Notification regarding review outcome (approval, modifications required etc) will be sent to PI.

● Study Closure: To close a study where Tulane’s IRB has deferred to another IRB, the PI must submit an Application for Closure (TU Form 602) to HRPO.

17.14 Special Topic—International Research

In addition to the usual requirements for Research involving Human Subjects, some unique issues are particularly vital for IRB review to protect Human Subjects in international populations. To this end, IRB review of Research that involves Human Subjects in other countries must include appropriate expertise for evaluation of the study in the context of the specific international setting(s) and study population(s).

Procedures required in Federal and University policies may differ from those normally followed outside the U.S. for Research Involving Human Subjects. These may stem from differences in language, cultural and social history, and social mores. In addition, foreign country policies such as the availability of national health insurance, philosophically different legal systems, and social policies may make U.S. forms and procedures inappropriate. Additional laws, regulations, and international directive may apply to Research conducted in foreign countries, and may require further protections for Research subjects.

If protections are deemed equivalent, requests to review or waive some standard elements of U.S. approvals may be considered. However, protections afforded to subjects must approximate those provided to subjects in the U.S. Investigators are encouraged to contact the IRB Chair of the appropriate IRB to discuss these issues.

International Research studies must adhere to recognized ethics codes such as: the Common Rule and the Declaration of Helsinki.

Consent and recruitment documents must be in the language that is readable and understandable by the subjects or an approved translation method may be used. Additionally, the following issues should be discussed in the IRB Application (TU Form 102) or be addressed in the IRB discussion:

● Benefits to the subject;
● Community leader;
● Culturally-sensitive to local area;
• Paternalism;
• Potential coercion;
• Genetics/homogeneity/validity to other populations;
• Language sensitivity;
• “Helicopter” Research (e.g., data/sample collection and leaving site with no follow-up);
• Infrastructure; and
• Justify use of this population.

17.15 Additional Requirements for Department of Defense (DoD) or Department of Navy (DoN) Collaborative Research

Tulane must assure that Research complies with additional U.S. Department of Defense (DoD) or the U.S. Department of Navy (DoN) requirements in the following instances:

• Tulane conducts, reviews, approves, oversees, supports manages or otherwise is contractually subject to regulation by the DoD or DoN; and/or

• Human subject research performed at Tulane using DoD-DoN property, facilities, or assets.

If these elements are met, refer to Tulane’s policy entitled “Human Subjects Protection: Additional Department of Defense (“DoD”) - Department of the Navy (“DoN”) Requirements” for additional details regarding compliance requirements.
18 Special Topics

18.1 Certificate of Confidentiality (CoC)

Certificates of Confidentiality are issued by the Federal government to protect identifiable Research information from forced Disclosure. They allow the Investigator and others who have access to Research Records to refuse to disclose identifying information on Research Participants in any civil, criminal, administrative, legislative, or other proceeding, whether at the Federal, State, or local level. CoCs may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation.

The certificate goes beyond the Consent Form (TU Forms 402; 403; and 407) in ensuring Confidentiality and anonymity. Without the certificate, Researchers can be required by a court-ordered subpoena to disclose Research results (usually as part of a criminal investigation of the subjects).

Any Research project that collects personally identifiable, sensitive information and that has been approved by an IRB is eligible for a Certificate. Federal funding is not a prerequisite for a Certificate.

18.1.1 Statutory Basis for Protection

Protection against compelled Disclosure of identifying information about subjects of biomedical, behavioral, clinical, and other Research is provided by the Public Health Service Act §301(d), 42 U.S.C. §241(d):

"The Secretary may authorize persons engaged in biomedical, behavioral, clinical, or other Research (including Research on mental health, including Research on the use and effect of alcohol and other psychoactive Drugs) to protect the Privacy of individuals who are the subject of such Research by withholding from all persons not connected with the conduct of such Research the names or other identifying characteristics of such individuals. Persons so authorized to protect the Privacy of such individuals may not be compelled in any Federal, State or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals."

18.1.2 Usage

Certificates of Confidentiality may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation. By protecting Researchers and institutions from being compelled to disclose information that would identify Research subjects, Certificates of Confidentiality help achieve the Research objectives and promote participation in studies by assuring Confidentiality and Privacy to subjects.

Any Investigator engaged in Research in which sensitive information is gathered from Human Subjects (or any person who intends to engage in such Research) may apply for a Certificate of Confidentiality. Research can be considered "sensitive" if it involves the collection of:

1. information about sexual attitudes, preferences, practices;
2. information about personal use of alcohol, Drugs, or other addictive products;
2. information about illegal conduct;
3. information that could damage an individual's financial standing, employability, or reputation within the community;
4. information in a subject's medical record that could lead to social stigmatization or discrimination; or
5. information about a subject's psychological well-being or mental health.

This list is not exhaustive. Researchers contemplating Research on a topic that might qualify as sensitive should contact the HRPO for help in applying for a certificate.

In the Consent Form (TU Forms 402; 403; and 407), Investigators should tell Research subjects that a Certificate is in effect. Subjects should be given a fair and clear explanation of the protection that it affords, including the limitations and exceptions noted above. Every Research project that includes Human Research Subjects should explain how identifiable information will be Used or Disclosed, regardless of whether or not a Certificate is in effect.

18.1.3 Limitations

The protection offered by a Certificate of Confidentiality is not absolute. A Certificate protects Research subjects only from legally compelled Disclosure of their identity. It does not restrict voluntary Disclosures.

For example, a Certificate does not prevent Researchers from voluntarily disclosing to appropriate authorities such matters as child abuse, a subject's threatened violence to self or others, or from reporting a communicable disease. However, if Researchers intend to make such Disclosures, this should be clearly stated in the Consent Form (TU Forms 402; 403; and 407) which Research subjects are asked to sign.

In addition, a Certificate of Confidentiality does not authorize the person to whom it is issued to refuse to reveal the name or other identifying characteristics of a Research subject if

1. The subject (or, if he or she is legally incompetent, his or her Legal Guardian) consents, in writing, to the Disclosure of such information;
2. Authorized personnel of DHHS request such information for audit or program evaluation, or for investigation of DHHS grantees or contractors and their employees; or
3. Release of such information is required by the FDA Act or regulations implementing that Act.

18.1.4 Application Procedures

Any person engaged in Research collecting sensitive information from Human Research Subjects may apply for a Certificate of Confidentiality. For most Research, Certificates are obtained from NIH. If NIH funds the Research project, the Investigator may apply through the funding Institute. However, even if the Research is not supported with NIH funding, the Investigator may apply for a Certificate through the NIH Institute or Center (IC) funding Research in a scientific area similar to the project.

If the Research is conducting a sensitive Research project that is covered by the AHRQ confidentiality statute [42 U.S.C. 299a-1(c) entitled “limitation on use of certain information”] or the Department of Justice confidentiality statute [42USC 3789g], then a CoC is not required.
If there is an Investigational New Drug Application (IND) or an Investigational Drug Exemption (IDE), the Sponsor can request a CoC from the FDA.

For more information, see the NIH Certificates of Confidentiality Kiosk (http://grants.nih.gov/grants/policy/coc/index.htm).

18.2 Mandatory Reporting of Abuse and Neglect

18.2.1 Definitions

**Abuse:** Is the infliction, attempted infliction, or, as a result of inadequate supervision, the allowance of the infliction or attempted infliction of physical or mental injury upon a Child or Elder by another person. It also entails the involvement of the Child in any sexual act with any other person; the involvement of the Elder in any unconsented sexual act with any other person; the aiding or toleration by the Parent or the caretaker of the Child/Elder's sexual involvement with any other person; the Child/Elder's involvement in pornographic displays; or any other involvement of a Child/Elder in sexual activity constituting a crime under the laws of this state.

**Elder:** means an adult over the age of 60.

18.2.2 Reporting Obligation of Abuse & Neglect

The Abuse and Neglect of Children, Neonates and Elders creates attendant human and financial costs to those that are Abused/Neglected as well as society at large. For this reason, Louisiana law requires that health care providers and practitioners (e.g., health, mental health, and social service practitioners) involved in the delivery of care report findings of suspected Abuse or Neglect to appropriate State and local agencies. [LA Children’s Code, Art. 601, et seq. (re. mandatory reporting for Children and Neonates; and LA R.S.14:403.2 (re. mandatory reporting for Elders)].

Consistent with Louisiana law, the HRPP has established a policy and procedure to protect the health, safety, and well-being of Children, Neonates and Elders who are involved as subjects in Research under the purview of Tulane’s IRB. It also establishes an attendant duty to notifying appropriate State and local agencies of instances of suspected Abuse and Neglect.

18.2.3 Confirming the Existence of Abuse or Neglect

During the consenting process, enrollment or Research activities, PIs, Investigators and/or Research staff may become aware of conditions that gives them cause to believe that potential Abuse or Neglect may exist of either (1) subjects who are Children or elders; and/or (2) to Children or elders of subjects.

It is imperative that the facts be reviewed and carefully considered before notifying appropriate governmental entities, especially in light of the gravity of the potential allegations that may be disclosed. For this reason, the following considerations should be had:

- **Confirming Abuse:**
  - Notwithstanding any claim of privileged communication, to the extent that a person **has cause to believe** that a Child or Elder's physical or mental health or welfare is endangered as a result of Abuse or that Abuse was a contributing factor in a Child or Elder's death or injury, he/she shall report the good faith suspicion to the appropriate State and local authorities in accordance with this policy and Louisiana law.
- In the event that a drug screen test of a mother is positive for an illegal controlled dangerous substance (“CDS”) and negative for a newborn, then this is deemed by the University to be Abuse. There is no need to retest for confirmation purposes due to the methodology currently used by the laboratory.

- **Confirming Neglect:** Notwithstanding any claim of privileged communication, to the extent that a person has cause to believe that a Neonate's physical or mental health or welfare is endangered as a result of Neglect, the following steps must be taken in conjunction with a Louisiana licensed physician:
  - Look for a positive drug screen test of a Neonate for an illegal CDS. Note well that there is no need to retest for confirmation purposes due to the methodology currently used by the laboratory. AND
  - A physician makes a positive medical diagnosis within thirty (30) days of birth that the Neonate either (i) is dependent upon the use of an illegal CDS; (ii) suffers from withdrawal symptoms from an illegal CDS; or (iii) a Neonate suffers from an illness, disease or condition in utero attributable to exposure to an illegal CDS.

### 18.2.4 What is the Reporting Procedure?

1. When a triggering event exists, mandatory reports are required by Louisiana law to report to Child Protective Services (“CPS”), Adult Protective Services (“APS”), the Department of Social Services, and/or Louisiana DHH their findings with respect to suspected Abuse or Neglect.
2. The PI (or delegate) is responsible for reporting all instances of Abuse and Neglect to CPS, as determined by this policy.
3. Reports of Abuse or Neglect or that such was a contributing factor in a Child's death, where the abuser is believed to be a Parent or caretaker, a person who maintains an interpersonal dating or engagement relationship with the Parent or caretaker, or a person living in the same residence with the Parent or caretaker as a spouse whether married or not, shall be made immediately to the local CPS or APS.
4. Reports in which the Abuse or Neglect is believed to be perpetrated by someone other than a caretaker, a person who maintains an interpersonal dating or engagement relationship with the Parent or caretaker, or a person living in the same residence with the Parent or caretaker as a spouse whether married or not, the caretaker is not believed to have any responsibility for the Abuse or Neglect shall be made immediately to a local or State law enforcement agency. Dual reporting to both the local CPS and/or APS unit and the local or State law enforcement agency is permitted.
5. Questions with respect to whether to report an incident to CPS should be referred to the University’s Office of General Counsel for assistance.

### 18.2.5 Immunity from civil or criminal liability

No cause of action shall exist against any person who in good faith makes a report or who cooperates in any investigation arising as a result of such report. State law protects the identity of all mandated reporters, who are given immunity from legal liability as a result of reports made in good faith.

Conversely, though, failure to report known instances of Abuse and/or Neglect may subject the offender to criminal prosecution. [LA R.S. 14:403(A)(1)].
18.3 Tulane Students and Employees as Subjects

When Tulane students and/or employees are being recruited as potential subjects, Researchers must ensure that there are additional safeguards for these subjects. The voluntary nature of their participation must be primary and without undue influence on their decision. Researchers must emphasize to subjects that neither their academic status or grades, or their employment, will be affected by their participation decision.

To minimize coercion, Investigators should avoid, whenever possible, the use of their students and employees in procedures which are neither therapeutic nor diagnostic. In these latter situations, Investigators should solicit subjects through means such as bulletin board notices, flyers, advertisements in newspapers, and announcements in classes or laboratories other than their own. When entering a classroom to recruit students and conduct Research (e.g. administer a survey), Investigators must do so at the end of the class period to allow non-participating students the option of leaving the classroom, thereby alleviating pressure to participate.

18.4 Student Research

18.4.1 Human Subjects Research and Course Projects

Learning how to conduct ethical Human Subjects Research is an important part of a student’s educational experience. Research activities that are designed as part of a course requirement for purposes of learning experience only and are NOT designed to develop or contribute to generalizable knowledge MAY not require IRB review and approval if all of the following conditions are true:

- Results of the Research are viewed only by the course instructor for teaching purposes and discussed within the classroom for teaching and learning purposes;
- Results of the Research are not made public through presentation (outside of the classroom) and are not published in paper or electronic format (e.g., cannot be made available on the internet, cannot be published in a journal, etc.);
- Research procedures are no more than Minimal Risk;
- Vulnerable populations are not targeted (e.g., Children under age 18, Prisoners, persons who are cognitively impaired, etc.);
- Data collected are recorded in such a manner that the subjects are not identifiable (images in videotapes and photographs and voices on audiotape are identifiable); and
- When appropriate, an informed consent process is in place.

Responsibility of the Course Instructor: The course instructor is responsible for communicating to the students the ethics of Human Subjects Research, for ensuring the protection of Human Subjects (including a process is in place for obtaining voluntary informed consent from Research subjects when appropriate), and for monitoring the students’ progress.

When designing a project, students should be instructed on the ethical conduct of Research and on the preparation of the IRB Application (TU Form 102) when such is required. In particular, instructors and students should:

- Understand the elements of informed consent;
Develop appropriate consent documents;
Plan appropriate strategies for recruiting subjects;
Identify and minimize potential risks to subjects;
Assess the risk-benefit ratio for the project;
Establish and maintain strict guidelines for protecting Confidentiality; and
Allow sufficient time for IRB review (if necessary) and completion of the project.

In making a determination of whether or not a class Research project requires IRB review, the instructor is encouraged to err on the side of caution and to contact the HRPO for assistance.

18.4.2 Individual Research Projects Conducted by Students

Independent study projects, senior theses, undergraduate Research projects, masters and advanced degree Research, and similar exercises that involve Human Subjects must be independently submitted for IRB review. It is important to keep in mind that any Human Subjects Research activity that will ultimately contribute to part or all of a thesis, dissertation, or other type of publication or presentation must go through the IRB review process prior to enrolling Human Subjects and collecting data. **IRB review cannot occur after a study has begun.**

Students and advisors should contact the HRPO with any questions.

Tulane policy and procedures, educational module, forms and related information can be found on the Tulane IRB Website at: [http://tulane.edu/asvpr/irb](http://tulane.edu/asvpr/irb).

18.4.3 Independent Study, Theses and Dissertations

These Research activities are considered to meet the Federal definition of Human Subject Research and should be independently submitted to the IRB. However, when students conduct Research as part of a course of study, a faculty member who services as the PI, ultimately is responsible for the protection of the subjects, even if the student is the primary Researcher and actually directs the project. Students are not routinely allowed to be PI(s). However, if appropriate and the student obtains special permission from their Department Head and Dean of their school acknowledging their approval as a PI then consideration will be given by the IRB. PIs are routinely required to be faculty. Advisers assume the responsibility for students engaged in independent Research, and instructors are responsible for Research that is conducted as part of a course.

Ordinarily, students may not serve as PIs. However, in limited circumstances, students may serve as PI (see Tulane’s policy entitled “Who Can be a PI?” for details).

18.5 Oral History

“Oral history” is a technique in which the researcher conducts a series of recorded interviews with the Participants in a particular historical event or period. Often, the intention is that these recordings become available to the public at a specified future period of time (e.g., frequently after a substantial delay) in order to convey historical insight.
In many cases, these interviews will be historical recollections of the character of a society or an institution rather than the interviewee's subjective perceptions. Such activities may or may not be considered human subjects research requiring the prospective review and approval of the IRB before commencing the activity pursuant to 45 CFR §46.101(b) (2) and §46.101(b)(3).

If in doubt, an oral history project should be submitted in advance to the HRPO to determine whether it is subject to IRB review or, conversely, whether it is exempt from review.

The threshold question in determining whether an oral history is subject to the Human Subject protections is whether the activity meets the definition of Research. A decision whether oral history or other activities solely consisting of open ended qualitative type interviews are subject to the policies and regulations outlined in an institution’s FWA and HHS regulations for the protection of Human Subjects Research is based on the prospective intent of the investigator and the definition of “research” under HHS regulations at 45 CFR §46.102(d); “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.” Interviews conducted with questionnaires and anonymous sources, from which generalized conclusions are drawn, fit the definition of Research. Open-ended, individualistic interviewing about events that have occurred in the past represents a fundamentally different form of research than federal regulations were intended to encompass.

Focus should be had on the prospective intent of the PI and the definition of Research (i.e., does it involve a “systematic investigation, including Research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.” [OHRP Guidance]

An activity is considered to not be an oral history and not Exempt if it satisfies both of the following requirements:

1. The activity involves a prospective Research plan which incorporates data collection, including qualitative data, and data analysis to answer a Research question; and

2. The activity is designed to draw general conclusions (i.e., knowledge gained from a study may be applied to populations outside of the specific study population), inform policy, or generalize findings.

When reviewing activity to determine whether it is an oral history that qualifies for Exempt Review, the following general principles may be useful for evaluative purposes:

1. Oral history activities, such as open ended interviews, that ONLY document a specific historical event or the experiences of individuals without intent to draw conclusions or generalize findings would NOT constitute Research.

   Example: An oral history video recording of interviews with holocaust survivors is created for viewing in the Holocaust Museum. The creation of the video tape does NOT intend to draw conclusions, inform policy, or generalize findings. The sole purpose is to create a historical record of specific personal events and experiences related to the Holocaust and provide a venue for Holocaust survivors to tell their stories.

2. Systematic investigations involving open-ended interviews that are designed to develop or contribute to generalizable knowledge (e.g., designed to draw conclusions, inform policy, or generalize findings) WOULD constitute Research.
**Example:** An open ended interview of surviving Gulf War veterans to document their experiences, and to draw conclusions about their experiences, inform policy, or generalize findings.

4. Oral historians and qualitative Investigators may want to create archives for the purpose of providing a resource for others to do Research. Since the intent of the archive is to create a repository of information for other Investigators to conduct Research.

**Example:** Open ended interviews are conducted with surviving Negro League Baseball players in order to create an archive for future Research. The creation of such an archive would constitute Research since the intent is to collect data for future Research.

Investigators are advised to consult with the HRPO regarding whether their oral history project requires IRB review.

### 18.6 Public Registration of Clinical Trials

The FDA requires that certain trials be publicly registered at “clinicaltrials.gov” before any subjects are enrolled. [See PHSA; Section 13 of MMA; 21 CFR §312; 42 USC 282(i)]. The URL for the registration site is: [https://register.clinicaltrials.gov/](https://register.clinicaltrials.gov/)

#### 18.6.1 Who Must Register?

The responsible party for registering applicable clinical trials is the Sponsor of the clinical trial, which means the person who initiates a clinical investigation.

- For investigator-initiated trials, the lead PI responsible for initiating, conducting and coordinating the overall clinical trial is responsible for registration;
- For Sponsor-initiated trials the Sponsor is responsibility for registration;
- For trials Sponsored or funded wholly or in part by the NIH the grantee is responsible for registration; and
- For trials associated with IND or IDE applications with the FDA the IND/IDE holder is responsible for registration.

The Sponsor, grantee, contractor, or awardee may designate the principal investigator of a clinical trial as the responsible party, provided that the principal investigator is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements for submitting information under the law.

Once a trial is registered, the responsible person also must ensure on an ongoing basis that the information is complete, accurate and updated. This includes reviewing the listing and making necessary changes every 6 months or more frequently if significant changes occur. You are also responsible for noting when enrollment ceases.

If unclear who is responsible registering an applicable clinical trial, investigators should consult with the Sponsor, funding agency, and/or other study investigators to define who the responsible party will be.

#### 18.6.2 Which Studies Must Be Registered?

Registration is required for any research study that:
• Prospectively assigns Human Subjects to intervention and at least one concurrent control or comparison groups; AND
• Uses a Drug, Biologic, or Device as the intervention or control/comparison; AND
• Studies the safety, efficacy or cause-and-effect relationship between an intervention and a health outcome

The registration requirement does not apply to:

• The use of FDA approved, marketed products used in the course of medical practice;
• Phase I Clinical Investigations of Drugs or Biologics;
• Small clinical trials to determine the feasibility of a device or clinical trial to test prototype devices where the primary outcome measure relates to feasibility and not to health outcomes;
• FDA required pediatric post-marketing surveillance of devices;
• Purely observational studies, meaning those studies where the assignment of the intervention is not at the discretion of the investigator; and/or
• Investigators and Sponsors are encouraged to register all clinical trials to ensure they meet the publication requirements of the International Committee of Medical Journal Editors (‘ICMJE’) and to promote transparency in clinical research.

18.6.3 When Must the Information Be Submitted?

Information about new Protocols open for enrollment must be registered not later than 21 days after Protocol approval. [42 U.S.C. 282(j)(3)]. Supplemental information can be submitted at 30-day intervals. The FDA strongly encourages you to update information about trials that are unexpectedly closed (e.g., clinical hold) within 10 days after the closing or sooner if possible.

18.6.4 How To Register a Clinical Trial?

Search ClinicalTrials.gov to ensure that the trial is not already listed. NIH-sponsored clinical trials and many industry-sponsored trials have already been registered on this site. If the trial is not listed, continue with registration.

Establish an account with the ClinicalTrials.gov. Within 2 business days, you will receive an E-mail message from ClinicalTrials.gov containing your login name and temporary password.

Once you have received your login information, register the trial. This process will take approximately 1 hour, and it will be helpful to have the Protocol, informed consent document, and IRB approval (if available) on hand. IRB approval is not required to register a trial. Note that this system offers the option to save data if you do not have time to complete the entire process.

Some suggestions for completing certain items that you might not have available are:

• Unique Protocol ID: The Tulane IRB number is recommended. An IRB number can be generated by starting an application in the IRBNet system. IRB approval is not required to register a trial. The IRB number is also used in the Board Approval Number field.
• Secondary IDs: The grant number, funding agency number or other funding source number is recommended.

• Board Name (Full name of the approving human subjects review board): Tulane University Biomedical Institutional Review Board

• Board Affiliation (Official name of organizational affiliation of the approving human subjects review board): Tulane University Biomedical Institutional Review Board

• Board Contact (Contact information for the human subjects review board):
  Name: Roxanne R. Johnson, Director
  Phone: 504-988-2665
  Email: rjohnson@tulane.edu
  Address: 1440 Canal Street, Suite 1705, New Orleans, LA 70112

Oversight Authorities: should always include United States: Institutional Review Board; other oversight authorities such as the FDA may also apply depending on the clinical trial

When the template is complete, hit “Submit” for release of the content to ClinicalTrials.gov

Information should be reviewed and updated as needed every 6 months or more frequently if changes occur

18.6.5 What Information Must Be Submitted?

The following are examples of information to be submitted:

• Descriptive Information
  • Brief Title (in lay language)
  • Brief Summary (in lay language)
  • Study Design/Study Phase/Study Type
  • Condition or Disease
  • Intervention

• Recruitment Information
  • Study Status Information including
  • Overall Study Status (e.g., recruiting, no longer recruiting)
  • Individual Site Status
  • Eligibility Criteria/Gender/Age

• Location and Contact Information
  • Location of Trial
  • Contact information (includes an option to list a central contact person for all trial sites)

• Administrative Data
  • Unique Protocol ID Number
  • Study Sponsor
  • Verification date
18.6.6  Who Receives the Submitted Information?

The DHHS Secretary acting through the NIH Director receives information submitted to ClinicalTrials.gov.

18.6.7  Who Can Access the Registered Information?

Studies will be made available to the public through ClinicalTrials.gov within two to five days after submission by the Sponsor. Except for the IND number, serial number, and FDA center designation, all information submitted through the PRS is made available to the public.

18.6.8  Must Information Be Included About Foreign Trial Sites?

Yes, a Sponsor must include information about foreign trials when those trials are conducted under an IND submitted to FDA and the trial meets the criteria for submission to the Clinical Trials Data Bank. [42 U.S.C. 282(j)(3)]. Sponsors may voluntarily conduct a foreign trial under the IND regulations. Sponsors are not required to submit information to the Clinical Trials Data Bank when a foreign trial is not conducted under an IND.

18.6.9  Can Intermediaries Act on Behalf of a Sponsor?

Yes. For example, in some cases a Sponsor might want to contract with an information management company to serve as an intermediary in preparing data for inclusion in ClinicalTrials.gov. The information management company, when authorized by the Sponsor, could act on behalf of the Sponsor for this purpose.

18.6.10  Can Sponsors Designate Multiple Individuals to Be Data Providers?

Yes. When Sponsors register to become a PRS data provider, they will be given information, including instructions, for creating additional users for their accounts. A Sponsor can control access to the account by designating users and administrators for the account.

18.6.11  What are the NIH Requirements for ClinicalTrials.gov Registration Information in Applications and Progress Reports?

On September 27, 2007 Congress enacted U.S. Public Law 110-85 (also known as H.R. 3580, or Food and Drug Administration Amendments Act of 2007). This act mandates the expansion of ClinicalTrials.gov, expands the required submission elements and establishes penalties for not listing a trial. Investigators and Sponsors must ensure that applicable Drug, Biologic and Device trials are registered within 21 days of enrollment of the first subject and preferable before first subject enrollment. The legislation also requires applications or progress reports for any clinical trials required to be registered which are funded in whole or in part by a grant from any agency of the DHHS to contain specific information certification registration in ClinicalTrials.gov.

18.6.12  How do the FDA registration requirements affect NIH funded studies?

- Competing renewal applications that include studies that are required to be registered must include as part of the Human Subjects Section of the Research Plan the following items:
  - A statement that “This application includes a trial which requires registration in ClinicalTrials.gov;”
  - The National Clinical Trial (“NCT”) number (i.e. the ClinicalTrials.gov number);
  - Brief Title as listed in ClinicalTrials.gov; and
The name of the individual or entity responsible for registering the study (responsible party) for each study being conducted under the application. (As grantee, Tulane University designates the lead Investigator of the trial as the responsible party.)

If the application does not include studies that are required to be registered the Human Subjects Section of the Research Plan should include a statement that “This application does not include a trial which requires registration in ClinicalTrials.gov.” These requirements apply to all competing applications submitted to the NIH on or after January 25, 2008.

New applications that include studies that are required to be registered must include as part of the Human Subjects Section of the Research Plan a statement that “This application includes a trial which requires registration in ClinicalTrials.gov.” The study would then need to be registered and the National Clinical Trial (“NCT”) number, Brief Title as listed in ClinicalTrials.gov and the individual or entity responsible for registering the study (responsible party) for each study being conducted under the application as part of the Just-In-Time (“JIT”) information. If a new application does not include studies that are required to be registered the Human Subjects Section of the Research Plan should include a statement that “This application does not include a trial which requires registration in ClinicalTrials.gov.”

Non-competing progress reports that include studies that are required to be registered must include as part of the Human Subjects Section of the Progress Report the following items:

- A statement that “This application includes a trial which requires registration in ClinicalTrials.gov;”
- The National Clinical Trial (NCT) number (i.e. the ClinicalTrials.gov number);
- Brief Title as listed in ClinicalTrials.gov; and
- The name of the individual or entity responsible for registering the study (responsible party) for each study being conducted under the application. (As grantee, Tulane University designates the lead investigator of the trial as the responsible party.)

If the application does not include studies that are required to be registered the Human Subjects Section of the Research Plan should include a statement that “This application does not include a trial which requires registration in ClinicalTrials.gov.” These requirements apply to all non-competing progress reports with budget start dates of April 1, 2008 or later (applications due on or after 2/1/08).

**18.6.13 Do the FDA regulations have any special requirements for IND, IDE or BLA studies?**

Studies conducted under an IND or IDE must include in the informed consent documents and the informed consent process a statement that clinical trial information for the study has been or will be submitted for inclusion in ClinicalTrials.gov as required by FDA regulations.

A certification must accompany human Drug, Biological, and Device product submissions made to FDA. At the time of submission of an IND, IDE or BLA application or submission of a report, amendment, supplement or resubmission, such application or submission must be
accompanied by a certification that all applicable requirements related to clinical trial registration have been met. Where available, such certification must include the appropriate National Clinical Trial (“NCT”) numbers.

The official certification form, Form FDA 3674 entitled “Certification of Compliance with Requirements of ClinicalTrials.gov Data Bank”, is available on FDA’s Web site.

For Sponsor held INDs, IDEs and BLAs the Sponsor must provide the certification. For investigator held INDs, IDEs and BLAs the individual holding the IND, IDE or BLA must provide the certification.

18.7 Genetic Studies

Genetic Research studies may create special risks to Human Subjects and their relatives. These involve medical, psychosocial, and economic risks, such as the possible loss of Privacy, insurability, and employability, change in immigration status and limits on education options, and may create a social stigma. Knowledge of one’s genetic make-up may also affect one’s knowledge of the disease risk status of family members.

1. In studies involving genetic testing, several questions need to be addressed, including:
   a. Will test results be given?
   b. Will disease risk be quantified, including the limits on certainty of the testing?
   c. Will a change in a family relationship be disclosed, such as mistaken paternity?
   d. Does the subject or family member have the option not to know the results? How will this decision be recorded?
   e. Could other clinically relevant information be uncovered by the study? How will Disclosure of this added information occur?
   f. Do any practical limitations exist on the subject's right to withdraw from the Research, withdraw data, and/or withdraw DNA?
   g. Is the subject permitted to participate in the study while refusing to have genetic testing (such as in a treatment study with a genetic testing component)?

2. For DNA banking studies, several questions need to be addressed, including:
   g. Will DNA be stored or shared? If shared, will the subject's identity be known by the new recipient Investigator?
   h. Will the subject be contacted in the future by the Investigator to obtain updated clinical information?
   i. How can the subject opt out of any distribution or subsequent use of his/her genetic material?

18.8 Research Involving Coded Private Information or Biological Specimens

Tulane policy is based on the OHRP guidance document entitled, “Guidance on Research Involving Coded Private Information or Biological Specimens” (August 10, 2004 http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf). This document:
• Provides guidance as to when Research involving Coded Private Information or specimens is or is not Research involving Human Subjects, as defined under HHS regulations for the protection of Human Subjects Research [45 CFR part 46];

• Reaffirms OHRP policy that, under certain limited conditions, Research involving only Coded Private Information or specimens is not Human Subjects Research; and

• Provides guidance on who should determine whether Human Subjects are involved in Research.

In general, Private Information or specimens are considered to be individually identifiable when they can be linked to specific individuals by the Investigator(s) either directly or indirectly through coding systems. Private information or specimens are not considered to be individually identifiable when they cannot be linked to specific individuals by the Investigator(s) either directly or indirectly through coding systems.

Research involving only Coded Private Information (or specimens) do not involve Human Subjects if the following conditions are both met:

1. The Private Information (or specimens) were not collected specifically for the currently proposed Research project through an interaction or intervention with living individuals; and

2. The Investigator(s) cannot readily ascertain the identity of the individual(s) to whom the Coded Private Information (or specimens) pertains. Example of how this might arise include:
   a. The key to decipher the Code is destroyed before the Research begins;
   b. The Investigators and the holder of the key enter into an agreement prohibiting the release of the key to the Investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement) or pursuant to a data use agreement;
   c. There are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the Investigators under any circumstances, until the individuals are deceased; or
   d. There are other legal requirements prohibiting the release of the key to the Investigators, until the individual(s) is deceased.

In some cases an Investigator who Obtains Coded Private Information (or specimens) about living individuals under one of the conditions cited in 2(a)-(d) above may either (1) unexpectedly learn the identity of one or more living individuals, or (2) for previously unforeseen reasons, now believe that it is important to identify the individual(s). If, as a result, the Investigator knows, or may be able to readily ascertain, the identity of the individuals to whom the previously Obtained Private Information (or specimens) pertains, then the Research activity now would involve Human Subjects. Unless this Human Subject Research is determined to be Exempt (see Section 3.4), IRB review of the Research would be required. Informed consent of the subjects also would be required unless the IRB approved a waiver of informed consent (See Section 5.9).
18.8.1 Who Determines If Coded Private Information (or Specimens) Constitutes Human Subjects Research

The PI in consultation with the IRB Chair or HRPO Director will determine if the Research involving Coded information or specimens requires IRB review. If the request is verbal (by phone or in person) or by E-mail, it is the PI’s responsibility to maintain documentation of such a decision. If the PI submits a formal submission, the request must include sufficient documentation of the activity to support the determination. Formal submissions will be responded to in writing and a copy of the submitted materials and determination letter/E-mail will be kept on file.

18.9 Case Reports Requiring IRB Review

In general, an anecdotal report on a series of patients seen in one’s own practice and a comparison of these patients to existing reports in the literature is not Research and would not require IRB approval. Going beyond one’s own practice to seek out and report cases seen by other clinicians creates the appearance of a systematic investigation with the intent to contribute to generalizable knowledge and therefore would be considered Research and would require IRB approval.
19 Glossary

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]. See Section 7.2 for details.

Abuse: is the infliction, attempted infliction, or, as a result of inadequate supervision, the allowance of the infliction or attempted infliction of physical or mental injury upon a Child or Elder by another person. It also entails the involvement of the Child in any sexual act with any other person; the involvement of the Elder in any unconsented sexual act with any other person; the aiding or toleration by the Parent or the caretaker of the Child/Elder's sexual involvement with any other person; the Child/Elder's involvement in pornographic displays; or any other involvement of a Child/Elder in sexual activity constituting a crime under the laws of this state. See Section 18.2.1 for details.

Adverse Device Effect (or “ADE”): is any AE or adverse effect caused by or associated with the use of a Device that is Unanticipated and has not been included in the Protocol or the Investigator’s brochure. See Section 7.5.2 for details.

Adverse Events (or “AE”): is any untoward physical or psychological occurrence in a Human Subject participating in Research, including any abnormal sign (e.g., abnormal physical exam or laboratory finding, symptoms or disease associated with the Research or the use of a medical investigational Test Article), symptom, or disease, temporarily associated with the Subject’s participation in the Research. An AE does not necessarily have to have a causal relationship with the Research, or any risk associated with the Research or the Research intervention, or the assessment. See Section 8.2 for details.

Affiliated IRB Member: is an employee or agent of Tulane University (or a member of that person’s immediate family). Affiliated members include, but are not limited to individuals who are: Full- or part-time employees; current students; members of any governing panel or board of the institution; paid or unpaid consultants; health care providers holding credentials to practice at the institution; and, volunteers working at the institution on business unrelated to the IRB. See Section 2.7.1 for details.

Agent(s): are chemical agents that affects the function of living things. See Section 7.2 for details.

Allegation of Non-Compliance: is defined as an unproved assertion of Non-Compliance. See Section 10.2 for details.

Alternate Member: is an individual who has the experience, expertise, background, professional competence, and knowledge comparable to that of the primary IRB member(s) whom the alternate would replace. See Section 2.7.1 for details.

Approved (or “Approved,” “Approval,” or “IRB Approval”): means the determination by the IRB that the investigation has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and other institutional and Federal regulations. The Research may begin as of the IRB approval date. [DHHS 45 CFR §46.102(h); FDA 21 CFR §56.103(m)]. See Section 3.10.1 for details.
Approval in Principal: is IRB approval, as requested by a Sponsor, without the IRB having reviewed all of the study procedures and consent documents. [see (45 CFR §46.118)]. See Section 3.10.5 for details.

Assent: means a Child’s affirmative agreement to participate in Research. Mere failure of a Child to object may not, absent affirmative agreement, be construed as Assent. [FDA 21 CFR §50.3(n)]. See Section 6.9.1 for details.

Authorization (or “HIPAA Authorization”): for HIPAA purposes, is a written document completed and signed by the individual that allows use and Disclosure of PHI for specified purposes, which are generally other than treatment, payment, or health care operations of a Covered Entity.[45 CFR §164.501 and §164.508]. See Section 16.4 for details.

Federal-Wide Assurance (“Assurance” or “FWA”): is a written commitment by an institution to protect Human Subjects participating in Research. Under Federal regulations, any institution conducting or engaged in federally supported Research involving Human Subjects must obtain an Assurance in accordance with 45 CFR §46.103. This requirement also applies to any collaborating “performance site” institutions. Under 45 CFR §46.102 (f), an institution is “Engaged in Research” (as defined below) whenever its employees or Agents either intervene or interact with living individuals for Research purposes; or obtain, release, or access, Individually Identifiable Private Information for Research purposes. See Section 1.4 for details.

Blinded: a study is considered to be Blinded if when it is designed to compare two or more interventions in which the Investigator, the subjects, or some combination thereof, do not know the treatment group assignments of individual subjects. A Blinded study sometimes is called a masked study design.

Biologic: a substance made from a living organism or its products and used in the prevention, diagnosis, or treatment of certain health conditions. See Section 7.2 for details.

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. See Section 7.2 for details.

Case History (or “Case Histories”): is a record of all observations and other data pertinent in the investigation on each Research subject. A PI is required to prepare and maintain adequate and accurate Case Histories. Case Histories include the case report forms and supporting data (e.g., signed and dated consent forms), and medical records (e.g., physician progress notes, the subject’s hospital chart(s), nurses’ notes, etc). The Case History for each subject must document that informed consent was obtained prior to participation in the study. See Section 4.12.1 for details.

Child (or “Children”): are persons who have not attained the legal age for consent to treatments or procedures involved in the Research, under the applicable law of the jurisdiction in which the Research will be conducted. [DHHS 45 CFR §46.402(s); FDA 21 CFR §50.3(o)].

According to Louisiana Law, the legal age for consent for treatment or medical procedures is 18 years or older. [LA Children’s Code 116; LA R.S. 40:1095]. Louisiana law is silent with respect to the legal age to consent with respect to Research. For purposes of these SOPs, any person
who is under the age of 18 generally is unable to consent for him/herself. Several important exceptions exist under Louisiana law that effectively treat Children as adults and gives them the capacity to consent to their own medical care and to participate in Research. They include the following:

- For a Child to receive medical and/or surgical care at a hospital and/or to receive physicians’ services [LA R.S. 40:1095]. This may or may not overlap with the proposed Research;
- If a Child is emancipated by marriage. Regardless of age, a Child is fully emancipated upon his or her marriage [LA Children’s Code Art 379];
- If a Child is judicially emancipated. This requires a court order for Child older than 16 years of age [LA Children’s Code Art 366 and 1922];
- If a Child is emancipated by authentic act. This requires a Child older than 16 years of age and the Child’s Parents to execute a written document of emancipation, signed before a 2 witnesses and a notary [LA Children’s Code Art 368];
- If a Child seeks to be treated for venereal disease [LA R.S. 40:1065.1]; and
- If a Child seeks to be treated for drug abuse [LA R.S. 40:1096].

Because Louisiana law does not specifically address consent of Children with majority status to Research, the University’s IRB will review issues of consent related to enrollment of these Children in Research on a case-by-case basis. See Section 6.9.1 for details.

**Clinical Investigation:** 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]. See Section 7.2 for details.

**Coded:** means (1) Individually Identifiable Private Information (e.g., name or social security number) that would enable the Investigator to readily ascertain the identity of the individual to whom the Private Information (or specimens) pertains has been replaced with a number, letter, symbol, or combination thereof (i.e., the Code); and (2) a key to decipher the Code exists, enabling linkage of the Individually Identifiable Private Information (or specimens). See Section 16.4 for details.

**Common Rule:** refers is the “Federal Policy for the Protection of Human Subjects” that provides for the primary source of regulation of Research. It has been adopted by a number of Federal agencies. Although the Common Rule is codified by each agency separately, the text is identical to Department of Health and Human Services (“DHHS”) regulations contained in 45 CFR 46 Subpart A. For the purposes of the HRPP, references to the Common Rule will cite the DHHS regulations. See Section 1.4 for details.

**Confidentiality:** methods used to ensure that information obtained by Researchers about their Research subjects is not improperly divulged. Do not confuse this Research term with HIPAA Privacy requirements. See Section 3.7.5.1 for details.

**Consultant:** is an individual with competence in a special area that the IRB has invited to assist in the review of issues which require expertise beyond or in addition to the availability on the
IRB. These individuals do not count for IRB quorum purposes and cannot vote on any issue before the IRB [45 CFR §46.107(f)]. See Section 2.9 for details.

**Continuing Non-Compliance:** is defined as a pattern of Non-Compliance that, in the judgment of the RCO or convened IRB, suggests a likelihood that instances of non-compliance will continue without intervention. Continuing Non-Compliance also includes failure to respond to a request to resolve an episode of Non-Compliance. See Section 10.2 for details.

**Contract Research Organization (or “CRO”):** means a person that assumes, as an independent contract with the Sponsor, one or more of the obligations of a Sponsor (e.g., design of a Protocol, selection or monitoring of Investigators, evaluation of reports, and preparation of materials to be submitted to regulatory agencies. [FDA 21 CFR §312.3(b)]. See Section 11.2 and 16.7 for details.

**Covered Entity:** for HIPAA Privacy purposes, is the term applied to institutions that must comply with the HIPAA Privacy and Security Rule. They include: health plans, health care clearinghouses; and health care providers. [DHHS 45 CFR §160.103; 45 CFR §164.504]. See Section 16.4 for details.

**Convened IRB Review (or “Convened IRB”):** means review by a fully convened IRB. See Section 3.6 for details.

**Cooperative Research:** is defined as Research conducted in cooperation with and at a performance site of an institution or facility that is not owned or operated by Tulane or TUHC or that does not fall under Tulane IRB’s authority. An Off-Site Institution or Off-Site Facility may be domestic or international and may or may not have its own IRB. See Section 17.3 for details.

**Dead Fetus:** is a Fetus that exhibits neither a heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord, if still attached. [DHHS 45 CFR 46§202(a)]. See Section 6.6.1 for details.

**Deferred with Minor Modification:** is a situation where the IRB cannot approve the Research as submitted or where the Proposal and/or Consent Form require minor revisions (e.g., wording changes, with replacement language provided). For Proposals submitted for Convened IRB Review, the needed revisions are agreed upon at the IRB meeting. For Proposals submitted Expedited Review, the needed revisions are designated by the reviewer(s). None of the required modifications can be related to the regulatory criteria for approval. These revisions are presented to the PI for incorporation by simple concurrence. Revisions must be made exactly as designated by the IRB or reviewer(s). See Section 3.10.2.1 for details.

**Deferred with Major Modification:** is a situation where the IRB cannot approve the Research as submitted because (1) the Proposal and/or Consent Form require major modification or clarification; or (2) insufficient information is provided to adequately judge the Protocol application (e.g., the risks and benefits cannot be assessed with the information provided). IRB approval of the proposed Research must not occur until subsequent review of the material the PI submitted by the convened IRB or the expedited reviewer(s). See Section 3.10.3.1 for details.

**De-Identified Information:** for HIPAA Privacy purposes, Health Information that does not identify an individual and with respect to which there is no reasonable basis to believe that the information can be used to identify an individual. If information is de-identified, it no longer is subject to the Privacy Rule and exempt from HIPAA. [45 CFR §164.514(a) and (b); 45 CFR
§164.502(d)(permitted uses and Disclosures of De-Identified Information]. See Section 16.4 for details.

**Delivery**: means complete separation of the Fetus from the woman by expulsion, extraction, or any other means. See Section 6.6.1 for details.

**Deviations (or “Protocol Deviation”)**: is a violation of the Protocol that is Unanticipated and happens without any prior agreement (e.g., a Protocol visit scheduled outside Protocol window, blood work drawn outside Protocol window, etc.). The IRB will review these reports for frequency and may audit any Protocol reporting frequent Deviations. See Section 9.2 for details.

**Device (or Medical Device)**: is an instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related Test Article, including a component part, or accessory which is (a) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in humans, or (b) intended to affect the structure or any function of the body, and which does not achieve any of its primary intended purposes through chemical action within or on the body, and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes. See Section 7.5.2 for details.

**Disapproved (or “Disapproval”)**: means that the IRB cannot approve the Protocol as written. See Section 3.10.4 for details.

**Disclosure (or “Disclosure of PHI”)**: for HIPAA Privacy purposes, a Disclosure is the release, transfer, provision of access to, or divulging in any other manner IIHI outside of the Covered Entity. [45 CFR §164.501]. See Section 16.4 for details.

**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]. See Section 7.2 for details.

**Distribute (or Distribution)**: means the delivery of a Drug or Device other than by Administering or Dispensing. See Section 7.2 for details.

**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]. See Section 7.2 for details.

**Elder**: means an adult over the age of 60. See Section 18.2.1 for details.

**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. See Section 7.4.3 for details.
Engaged (or “Engaged in Research”): an institution is engaged in a Research project when its employees or Institutional Agents, for the purposes of the research project obtain: (1) data about the subjects of the Research through intervention or interaction with them; or (2) Individually Identifiable Private Information about the subjects of the Research or identifiable biological specimens; or (3) the informed consent of Human Subjects for the Research. Obtaining Individually Identifiable Private Information includes, but is not limited to: (1) observing or recording private behavior; (2) using, studying, or analyzing for Research purposes identifiable Private Information or identifiable specimens provided by another institution; and (3) using, studying, or analyzing for Research purposes Individually Identifiable Private Information or identifiable specimens already in the possession of the Investigators. See Section 17.3 for details.

Exceptions (or “Protocol Exceptions”): are circumstances in which the specific procedures called for in a Protocol are not in the best interests of a specific patient/subject (e.g., the patient/subject is allergic to one of the medications provided as supportive care). Usually it is a violation that is anticipated and happens with prior agreement from the Sponsor. See Section 9.2 for details.

Exempt Research (or “Exempt” or “Exempt Review”): is Research determined by the IRB to involve Human Subjects only in one or more of certain Minimal Risk categories [45 CFR §46.101(b)]. See Section 3.4 for details.

Ex-Officio Guest: Certain ex officio individuals (e.g., University Counsel, the RCO, and HRPO staff) regularly attend IRB meetings as ex officio guests. While they are not voting members of the IRB, they may participate in the IRB discussion and may provide additional information to the IRB. They need only sign a confidentiality agreement once. See Section 3.6.9 for details.

Expedited Research (“Expedited” or “Expedited Research”): is Research determined by the IRB to present no more than Minimal Risk to Human Subjects and involves only procedures in certain specific categories. Minor changes to previously approved Research during the period for which approval is authorized may also be approved through the Expedited process. [45 CFR §46.110 (b)]. See Section 3.5 for details.

Fetus: Is the product of conception (i.e., fusion of a human spermatozoa with a human ova) from the time of implantation until Delivery. [DHHS 45 CFR §46.202(c); LA R.S. 40:1299.35.1]. See Section 6.6.1 for details.

Financial Interest: is (1) aggregate investments (whether in the form of debt, stock or other equity ownership, options or warrants to purchase stock or other securities or similar instruments) with a value exceeding $10,000 or representing a five (5%) percent or greater interest in any entity, enterprise or trust; (2) royalties on any patent or other intellectual property interests with a value exceeding $10,000, unless paid by Tulane; or (3) income, salary or remuneration in cash or in kind, emoluments, benefits, gifts, honoraria, travel expenses, goods or services with a value exceeding $10,000. Financial Interest does not include holdings in mutual funds or other equity funds in which the day-to-day control of investments is held by a person not subject to any Tulane COI policy. This definition is extracted from the Institution’s COI policy contained in the Faculty Handbook, Part III, D, Part A. The definition in the Faculty Handbook shall prevail to the extent that there is a conflict. See Section 14.2 for details.

Finding of Non-Compliance: is an Allegation of Non-Compliance that is proven true or a report of Non-Compliance that is clearly true. (e.g., a finding on an audit of an unsigned consent
document, or an admission of an Investigator that the Protocol was willfully not followed would represent reports of non-compliance that would require no further action to determine their truth and would therefore represent findings of Non-Compliance.) See Section 10.2 for details.

**Guardian (or Legal Guardian):** means an individual who is authorized under applicable State or local law to consent on behalf of a Child to (a) general medical care when general medical care includes participation in Research; or (b) to participate in Research. [DHHS 45 CFR §46.402(e); FDA 21 CFR 50.3(s); LA. Children’s Code 116(12.1)(a)(i)(b)]. A Guardian of a Minor retains the duty and authority to (1) act in the best interests of the Minor, subject to residual Parental rights and responsibilities (if any); (2) make important decisions in matters having a permanent effect on the life and development of the Minor; and (3) to be concerned with the Minor’s general welfare. For Research conducted in jurisdictions other than Louisiana, the Research must comply with the laws regarding guardianship in all relevant jurisdictions where the Research will take place. See Section 6.9.1 for details.

**Health Agent:** Is an authorized representative legally acting for a person pursuant to a Durable Power of Attorney for Health Care (“Medical Power of Attorney”) or other legal document permitted within a jurisdiction that allows a person to appoint another person(s) to make medical decisions for the patient if the patient should become temporarily or permanently unable to make those decisions for himself/herself. Any adult (18 or older) can be granted this power. [LA R.S.40:1299.53(A)(13)]. See Section 6.9.1 for details.

**Health Information:** for HIPAA Privacy purposes, it means any information, whether oral or recorded in any form or medium, that: (1) is created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university, or health care clearinghouse; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual. [DHHS 45 CFR §160.103]. See Section 16.4 for details.

**Human Subject(s) Research:** means any activity that meets the definition of Research and involves Human Subjects as defined by either the Common Rule or FDA regulations. See Section 1.4 for details.

**Human Research Protection Program (“HRPP”):** Tulane’s HRPP is a comprehensive system to ensure the protection of Human Subjects participating in Research. The objective of this program is to assist the institution in meeting applicable ethical principles and regulatory requirements for the protection of Human Subjects in Research. See Section 1.4 for details.

**Human Subject (“Subject,” “Participant,” “Human Participant,” “Human Research Subject”):** a Human Subject is defined by the Common Rule as a living individual about whom an Investigator conducting Research obtains data through Intervention or Interaction with the individual or through Individually Identifiable Private Information. [DHHS 45 CFR §46.102(f); FDA 21 CFR §50.3(g); 21 CFR §56.102(e); 21 CFR §312.3(b)]. For purposes of this definition, the following definitions are germane:

- **“Interaction”** means communication or interpersonal contact between Investigator and subject. [DHHS 45 CFR §46.102(f)];
- **“Intervention”** means both physical procedures by which data are gathered (example, veni-puncture) and manipulations of the subject or the subject’s environment that are performed for Research purposes. [DHHS 45 CFR §46.102(f)]

For Research covered by FDA regulations [21 CFR Parts 50 and 56], Human Subject means an individual who is or becomes a Participant in a Clinical Investigation, either as a recipient of the Test Article or as a control. A subject may be in normal health or may have a medical condition or disease. [21 CFR §50.3(g), 21 CFR §56.102]. In the case of a Medical Device, a Human Subject/Participant also includes any individual on whose tissue specimen an Investigational Device is used or tested. [21 CFR §812.3(p)].

NOTE: The FDA definition of Human Subject differs according to the applicable regulation. [See 21 CFR §812.3(p), 21 CFR §50.3(g), §312.3(b), and §56.102(e)]. See Section 1.4 for details.

**Humanitarian Use Device (“HUD”):** the FDA defines HUD as a Device intended to benefit patients by treating or diagnosing a disease that affects fewer than 4,000 individuals in the U.S. per year. [FDA 21 CFR 814.3(n)]. See Section 7.5.7 for details.

**Hybrid Entity:** for HIPAA Privacy purposes, it is a single legal entity that (a) is a Covered Entity; (b) whose business activities include activities covered and not covered under the HIPAA Privacy Regulations; and (c) that designates health care components that will be subject to HIPAA. [45 CFR §164.103]. See Section 16.4 for details.

**Identifiable Information:** for research privacy purposes, this means information where the identity of the subject is or may readily be ascertained by the Investigator or associated with the information. This term should not be confused with IIHI used with HIPAA. See Section 3.7.5.1 for details.

**Individually Identifiable Health Information (“IIHI”):** for HIPAA Privacy purposes, this is information, including demographic information collected from an individual, that: (i) is created or received by a health care provider, health plan, employer, or health care clearinghouse; (ii) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual; and (iii) identifies the individual; or with respect to which there is a reasonable basis to believe the information can be used to identify the individual. [45 CFR §160.103]. This term should not be confused with “Individually Identifiable Private Information,” which is not covered by HIPAA. See Section 16.4 for details.

**Individually Identifiable Private Information:** is information where, for Research purposes, the identity of the subject is or may readily be ascertained by the Investigator or associated with the information. See Section 3.7.5.1 for details.

**Institutional Agent:** is all individuals performing Institutionally designated activities or exercising Institutionally delegated authority or responsibility under Tulane’s FWA. See Section 1.4 for details.

**Institutional Official (“IO”):** the University Vice President for Research (“VPR”) serves as the Institution’s IO for carrying out the HRPP. The IO is responsible for ensuring that the HRPP has the resources and support necessary to comply with all Federal regulations and guidelines that govern Human Subject Research. The IO is legally authorized to represent the Institution, is the
signatory official for all Assurances, and assumes the obligations of the Institution’s Assurance. See Section 1.4 for details.

**Institutional Review Board ("IRB"):** is an independent board(s) designated by the Institution to review, to approve the initiation of, and to conduct periodic review of Research involving Human Subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the Human Subjects. The IRB may be assigned other review functions as deemed appropriate by the Institution. This independent board is composed of medical, scientific, and non-Scientific Members. See Section 1.4 for details.

**Investigational Device:** as defined by the FDA, an Investigational Device is a Device that is the object of a clinical study designed to evaluate the safety or effectiveness of the Device. [21 CFR §812.3(g)]. Investigational Devices include transitional Devices [21 CFR §812.3(r)] that are objects of investigations. However, for the purposes of this document, an Investigational Device may be an approved Device that is being studied for an unapproved use or efficacy. See Section 7.5.2 for details.

**Investigational Device Exemption ("IDE"):** is an FDA-approval of the application for an exemption that permits an un-marked Device to be shipped for the purpose of doing Research on the Device. [See 21 CFR §812.1 and §812.2 for the scope and applicability]. See Section 7.5.2 for details.

**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)]

See Section 7.2 for details.

**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]. See Section 7.2 for details.

**Investigator:** is an individual under the direction of the PI who is involved in some or all aspects in the Research project, including (1) the design of the study; (2) conduct of the study; (3) analysis and interpretation of the collected data; (4) directly involved in seeking the voluntary informed consent of potential subjects; and (5) writing of resulting manuscripts. Investigators
can include physicians, scientists, nurses, Research staff members, administrative staff, teachers, and students. Investigators must be included on the **FDA Form 1572** and/or the **IRB Application** request signature page. While the FDA considers an Investigator and a PI to be synonymous, this document does not. [FDA 21 CFR §50.3(d); 21 CFR §56.102(h); 21 CFR §312.3(b)]. See Section 1.4 for details.

**Investigator Hold**: is a situation where an Investigator or Sponsor wishes to temporarily or permanently, stop some or all approved Research activities. Investigator Holds are not Suspensions or Terminations. (See Section 3.11.2).

**IRB Records**: See Section 4.3 for the definition.

**Form 1572 (or “FDA Form 1572” or “Statement of Investigator FDA Form”)**: is the form submitted by the PI to the Sponsor acknowledging their obligations in the conduct of the Research. PIs on treatment Protocols that involve an IND must complete FDA Form 1572. The FDA Form 1572 is the contract between the Investigator and the Federal government assuring that he or she will comply with FDA regulations. [21 CFR §312.53]. By signing the Form 1572, the Investigator assumes full responsibility for the study. See Section 3.6.5.

**Legally Authorized Representative**: is an individual, judicial, or other body authorized under applicable law to consent or otherwise provide permission on behalf of a subject, either prospectively or during the course of Research, to the subject's participation in the procedure(s) involved in the Research. [DHHS 45 CFR §46.102(c); FDA 21 CFR §50.3(l)]. For the purposes of this document, a Legally Authorized Representative includes a person appointed as a Health Agent, a court-appointed Legal Guardian of the person, as well as next-of-kin in the following order of priority unless otherwise specified by applicable State law: the subject’s spouse; adult Child(ren) of subject (18 years of age or older); Parent of subject; adult sibling(s) of subject (18 years of age or older); grandparent(s) of subject; or adult grandchild(ren) of subject (18 years of age or older). If there is more than one person within the above named class, the consent shall be given by a majority of those members of the class available for consultation.[LA R.S. 40:1299.53] Legally Authorized Representative should not be confused with Legal Guardian. See Section 6.9.1 for details.

**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]. See Section 7.4.2.2 for details.

**Limited Data Set**: for HIPAA Privacy purposes, is PHI that excludes specific direct identifiers of the individual or of relatives, employees or household members of an individual. A limited data set can only be used for the purposes of research, public health, or healthcare operations, and disclosed for the purpose of research. See Section 16.4 for details.

**Major Protocol Violation**: means a deviation that has an impact on subject safety, may substantially alter risks to subjects, may have an effect on the integrity of the study data, or may affect the subject’s willingness to participate in the study. Major violations can vary in the
degree of seriousness according to how the changes impact subject safety, the degree of non-compliance with the Federal regulations, state laws or Tulane’s policies or procedures, and the degree of foreknowledge of the event.

Examples of major violations include:

- Failure to obtain informed consent from the subject;
- Enrolling a subject who does not meet the inclusion and exclusion criteria;
- Performing study procedures that have not been approved by the IRB;
- Failure to perform a required laboratory test or procedure that could impact upon the safety of the subject;
- Continuing research activities after IRB approval has expired;
- Use of recruitment procedures that have not been approved by the IRB;
- Enrolling significantly more subjects than was proposed to and approved by the IRB; and
- Enrollment of a subject from a federally-defined vulnerable population (i.e. Children, Pregnant Women, Prisoners) without prior IRB approval for that vulnerable population.

See Section 9.7 for details.

Minor means any person under the age of 18 years. [LA Children’s Code Art 116]. Do not confuse the definitions of Minor (pertaining to a person’s age) with Child/Children (pertaining to a person’s ability to consent). See Section 6.9.1 for details.

Minor Protocol Violation: is one that does not impact subject safety, compromise the integrity of the study data, or affect the subject’s willingness to participate in the study. See Section 9.8 for details.

Minimum Necessary: for HIPAA Privacy purposes, this refers to the principle that any access (i.e., obtaining or using PHI by any means or in any medium) to PHI by Tulane workforce members should be limited to the minimum amount of PHI needed to accomplish the intended purpose of the use or Disclosure. [DHHS 45 CFR §164.502(b) and §.514(d)]. See Section 16.4 for details.

Minimal Risk (or “Minimum Risk”): means that the probability and magnitude of harm or discomfort anticipated in the Research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. See Section 3.7.1 and 3.81 for details.

Minimal Risk for Prisoners: is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. [DHHS 45 CFR §46.102(i); 45 CFR §46.303(d); FDA 21 CFR §50.3(k); 21 CFR §56.102(i)]. The definition of Minimal Risk for Prisoners contained in the Subpart C of the Federal regulations is different than the definition of Minimal Risk (for non-Prisoners). See Section 6.8.1 for details.

Neglect: of Neonate means a medical finding by a Louisiana licensed physician that a Neonate either is dependent upon or suffers from withdrawal symptoms from an illegal controlled dangerous substance (“CDS”). It also includes a medical finding by a physician that a Neonate
suffers from an illness, disease or condition attributable to the exposure of the newborn, in utero, of an illegal CDS. See Section 6.7.1 for details.

**Neonate**: means Newborn. [DHHS 45 CFR 46.202(d)]. See Section 6.7.1 for details.

**Non-Compliance**: is a failure to comply with any of the regulations and policies described in this document and failure to follow the determinations of the IRB. Non-Compliance may be minor or sporadic or it may be serious or continuing. See Section 10.2 for details.

**Non-Scientific Member**: is any IRB Member who has formal education and training in a discipline generally considered to be non-scientific (e.g. humanities, law, business) and/or is engaged in an occupation or role that is generally considered to be non-scientific (e.g. law enforcement, minister). See Section 2.7.1 for details.

**Non-Significant Risk Device (or NSR Device)**: is an Investigational Device other than a Significant Risk Device. See Section 7.5.2 for details.

**Non-Viable Neonate (or “Non-Viable Fetus”)**: is a Fetus ex utero that, although living, is not able to survive to the point of independently maintaining a heartbeat and respiration. [DHHS CFR 46.202(e)]. See Section 6.7.1 for details.

**Obtain (or “Obtaining”)**: means to receive or access Individually Identifiable Private Information (or identifiable specimens) for Research purposes. This includes an Investigator’s use, study, or analysis for Research purposes of Individually Identifiable Private Information (or identifiable specimens) already in the possession of the Investigator. See Section 3.7.5.1 for details.

**Off-Site Research (or “Non-Tulane Site,” “Off-Site Institution” or “Off-Site Facility” or “Off-Site Location”)**: is Human Subjects Research conducted under the auspices of Tulane’s IRB at performance sites that are not owned or operated by Tulane University or TUHC. See Section 17.3 for details.

**On-Site Research (or “Tulane Site”)**: is Human Subjects Research conducted under the auspices of Tulane’s IRB at performance sites that are owned or operated by Tulane University or TUHC. See Section 17.3 for details.

**Parent**: means a Child’s biological or adoptive parent. [FDA 21 CFR §50.3(p)]. See Section 6.9.1 for details.

**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. See Section 7.2 for details.

**Preparatory Research**: for HIPAA Privacy purposes, Preparatory Research is the method applied to developing or designing a research study. [45 CFR §164.512(i)(1)(ii)]. See Section 16.4 for details.

**Pregnant (or Pregnancy)**: is the period of time from confirmation of implantation (through any of the presumptive signs of pregnancy, such as missed menses, or by a medically acceptable pregnancy test), until expulsion or extraction of the Fetus. [DHHS 45 CFR §46.202(f)]. See Section 6.6.1 for details.
**Principal Investigator (“PI”):** is an individual who conducts research or under whose immediate direction research is conducted; or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team. While the FDA considers a PI and an investigator to be synonymous, this document does not. See Section 12.2 for details.

**Prisoner:** is any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing. [DHHS 45 CFR §46.303(c)]. See Section 6.8.1 for details.

**Privacy:** for Research purposes, having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. Do not confuse this Research term with HIPAA Privacy requirements. See Section 16.4 for details.

**Privacy Board:** for HIPAA Privacy purposes, Privacy Board is the term used to describe a board comprised of members of varying backgrounds and appropriate professional competencies, as necessary, to review individual’s private rights. It is an alternative to an IRB for privacy issues only. It cannot replace the IRB for Common Rule or FDA purposes. Tulane’s IRB shall serve as the Privacy Board for the Institution. See Section 16.4 for details.

**Private Information:** for research privacy purposes, this means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., a medical record). [45 CFR §46.102(f)]. Do not confuse this Research term with HIPAA Privacy requirements. See Section 3.7.5.1 for details.

**Proposal (or “Research Proposal”):** includes the complete packet of materials submitted to the IRB for review, including the Protocol, a description of the Research design and methodology as well a complete description of the procedures for the protection of Human Participants in the Research. See Section 4.2 for a listing of materials required to be submitted to the IRB.

**Protected Health Information (“PHI”):** for HIPAA Privacy purposes, PHI means IIHI that is transmitted or maintained in any form or medium (i.e., electronic, paper or verbal). [45 CFR §164.501]. PHI does not include IIHI in:

- Education records covered by the Family Educational Right and Privacy Act, as amended, 20 U.S.C. 1232g;
- Records described at 20 U.S.C. 1232g(a)(4)(B)(iv); and
- Employment records held by a covered entity in its role as an employer.

See Section 16.4 for details.

**Protocol:** is a document (including subsequent amendments) that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. A Protocol usually also gives the background and rationale for the trial, but this could be provided in other Protocol reference documents. [Good Clinical Practice: Consolidated Guidance (ICH-E6) (Protocol includes initial Protocol and Protocol amendments)]. See Section 1.4 for details.
Protocol Deviation(s): means a minor or administrative departure from the IRB-approved Protocol procedures (e.g., the Protocol, informed consent document, recruitment process or study materials) that was made without prior sponsor and IRB approval. It is an accidental or unintentional change to, or non-compliance with the Research Protocol that neither (a) increases the risk or decreases the benefit; and (b) significantly affects the subject’s rights, safety or welfare and/or the integrity of the Research data. Note that this term is not defined by the Common Rule or FDA regulations. See Section 9.1 for details.

Protocol Exception: means an impermanent (temporary) Protocol deviation that is pre-approved by the sponsor or funding agency, (and the FDA, if applicable, for investigational device studies) and the IRB prior to its implementation. Protocol Exceptions are generally for a single subject or, occasionally, a small group of subjects. The Protocol Exception is usually evaluated by both the sponsor or funding agency (and FDA, if applicable) and the IRB in order to determine that it does not increase the risk to the subject(s), or jeopardize the integrity of the research data. Documentation of sponsor (or FDA) pre-approval and IRB approval of the exception should be maintained in the investigator’s research study file. See Section 9.1 for details.

Protocol Violation(s): means an accidental or unintentional change to, or non-compliance with the IRB-approved procedures (e.g., the Protocol, informed consent document, recruitment process or study materials) without prior sponsor and IRB approval. Protocol Violations generally increases risk and/or decrease the benefit; affect the subject’s rights, safety or welfare and/or the integrity of the Research data. This term is not defined by the Common Rule or FDA regulations. See Section 9.1 for details.

Quorum: means the minimum number of persons required for the IRB to convene, transact business, deliberate and vote on all matters requiring IRB vote. For purposes of this document, a Quorum of the IRB is a majority (i.e., more than 50%) of the voting IRB membership for an IRB committee or subcommittee, including at least one member whose primary concern is in a non-scientific area as required by 45 CFR §46.108. If Research involves an FDA-regulated Test Article, a licensed physician also must be present for a Quorum to exist. See Section 3.6.7 for details.

Related (or “Possibly Related”): means that there is a reasonable possibility that the event, incident, experience or outcome may have been caused by the procedures involved in the Research, underlying disease, disorder, or condition of the Subject, or other circumstances unrelated to either the Research or any underlying disease, disorder, or condition of the Subject. Note that this is modified from the definition of associated with use of the drug in FDA regulations at 21 CFR §312.32(a). [OHRP 7/15/2007 Guidelines]. See Section 8.2 for details.

Research: is defined by the Common Rule as a “systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge.” [DHHS 45 CFR §46.102(d); FDA 21 CFR §50.3(c) & (g)].

FDA regulations define Research as meaning any experiment that involves a Test Article and one or more Human Subjects, and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act (the “FDA Act”), or need not meet the requirements for prior submission to the FDA under these sections of the FDA Act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a Research or marketing permit. The terms Research,
clinical Research, clinical study, study, and Clinical Investigation are synonymous for purposes of FDA regulations. [FDA 21 CFR §50.3(c), 21 CFR §56.102(c)].

- Experiments that must meet the requirements for prior submission to the FDA under section 505(i) of the FDA Act means any use of a Drug other than the use of an approved Drug in the course of medical practice. [21 CFR §312.3(b)].
- Experiments that must meet the requirements for prior submission to the FDA under section 520(g) of the FDA Act means any activity that evaluates the safety or effectiveness of a Device. [21 CFR §812.2(a)].
- Any activity in which results are being submitted to or held for inspection by FDA as part of an application for a Research or marketing permit is considered to be FDA-regulated Research [21 CFR §50.3(c), 21 CFR §56.102(c)].

See Section 1.4 for details.

**Research Financial Interest**: is any investments (whether in the form of debt, stock or other equity ownership, options or warrants to purchase stock or other securities or similar instruments) or interest in a Sponsor, research or healthcare related organization; royalties on any patent or other intellectual property interests, unless paid by Tulane; or income, salary or remuneration in cash or in kind, emoluments, benefits, gifts, honoraria, travel expenses, goods or services received from a Sponsor or research or healthcare related organization. Research Financial Interest does not include holdings in mutual funds or other equity funds in which day-to-day control of investments is held by a person not covered by any Tulane University Conflict of Interest policy. Please note that Research Financial Interest has no dollar or ownership thresholds; therefore, any interest related to a Sponsor or to the research must be disclosed, however small. This definition is extracted from the Institution’s COI policy contained in the Faculty Handbook, Part III, D, Part C. The definition in the Faculty Handbook shall prevail to the extent that there is a conflict. See Section 14.2 for details.

**Research Records (or “Investigator Records”)**: consist of records (as well as Case Histories or any data) prepared, created, gathered, or maintained by a PI, Investigator or research staff for Research Under the Auspices of the Institution. See Section 4.2 for details.

**Research Under the Auspices of the Institution**: this includes Research conducted at this Institution, conducted by or under the direction of any employee or Institutional Agent of this Institution (including students) in connection with his or her Institutional responsibilities, conducted by or under the direction of any employee or Institutional Agent of this Institution using any property or facility of this Institution, or involving the use of this Institution’s non-public information to identify or contact Human Subjects. See Section 1.4 for details.

**Researcher**: is the PI and/or Investigator. See Section 12.2 for details.

**Scientific Member**: is an individual who has formal education and training as a physician or other medical professional, and M.S. and/or Ph.D. level physical, biological, or social behavioral scientists. See Section 2.7.1 for details.

**Self-Sponsored (or “Investigator-Initiated” or “Investigator-Sponsored”)**: refers to a situation in which the individual Investigator is a Tulane Investigator and is the holder of the IND or IDE
and therefore assumes the duties of the Sponsor of the clinical Investigator under the applicable FDA regulations. See Section 13.2 for details.

**Serious Non-Compliance**: is defined as failure to follow any of the regulations and policies described in these SOPs or failure to follow the determinations of the IRB and which, in the judgment of the convened IRB, increases risks to Participants, decreases potential benefits, or compromises the integrity of the HRPP. Research being conducted without prior IRB approval is considered Serious Non-Compliance. See Section 10.2 for details.

**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]. See Section 7.2 for details.

**Significant Risk Device (“SR Device”)**: is an Investigational Device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a Human Subject;
- Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a Human Subject;
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presented a potential for serious risk to the health, safety, or welfare or a Human Subject;
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a Human Subject. See Section 7.5.2 for details.

**Sponsor**: is any person or party that provides funding to support the conduct of Research, usually through a specific statement of work and often with a related transfer of value to the Sponsor. A Sponsor does not actually conduct the investigation. A sponsor can be governmental (e.g., Federal, State or a local government) or private (e.g., a company, individual donor or private foundation), as well as self-sponsored (e.g., where Institution is responsible for funding the involved activity). The funding mechanism may be through a grant, contract or cooperative agreement. [FDA 21 CFR §50.3; 21 CFR §56.102(j); 21 CFR §312.3(b)]. See Section 13.2 for details.

**Substantive**: an action taken by an IRB that materially alters the substance and meaning of a Protocol, informed consent form or process, or Investigator status, including, but not limited to, Restriction, Suspension or Termination of a study or Investigator participation, and actions taken to prevent future occurrence(s) of the AE in Research. See Section 4.2 for details.

**Suspension (or “Suspend”)**: is an action of the convened IRB, IRB Chair and/or HRPO Director to temporarily cease some or all previously approved research activities to protect the rights and welfare of study Participants. Suspended Protocols remain open and require Continuing Review. See Section 3.11.1 for details.

**Termination (or “Terminate”)**: is an action of the convened IRB to stop all activities in a previously-approved research Protocol permanently. Terminated Protocols are considered closed and no longer require Continuing Review. See Section 3.11.1 for details.
**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)]. See Section 7.2 for details.

**Unanticipated Problems Involving Risk to Subjects or Others (or “Unanticipated Problem”):** means any incident, experience, outcome, or new information where all three exist:

1. Is unexpected;
2. Is related or Possibly Related to participation in the Research, and
3. Indicates that subjects or others are at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

For purposes of this definition, the following definitions are germane:

“**Others:**” means individuals other than Research Participants (e.g., Investigators, research assistants, students, the public, etc.).

See Section 8.2 for additional details.

**Use**: means, with respect to IIHI, the sharing, employment, application, utilization, examination, or analysis of such information within the organization that maintains such information. [45 CFR §164.501]. See Section 16.4 for details.

**Viable Neonate (or “Viable Fetus”):** means a Fetus that is able, after Delivery, to survive to the point of being able to independently maintain a heartbeat and respiration (given the benefit of available medical therapy). [DHHS 45 CFR §102(c) & (l); 45 CFR §46.202(h)]. See Section 6.7.1 for additional details.

**Vulnerable Population (or “Vulnerable Subjects”):** this includes the following classes of potential or actual Research subjects: Children, Prisoners, Pregnant Women, mentally-disabled persons, or economically- or educationally-disadvantaged persons. See Section 6.3 for details.

**Waiver of Authorization (or “Waiver of HIPAA Authorization”):** for HIPAA Privacy purposes, this is a means of requesting approval from an IRB or Privacy Board rather than asking each Research subject for an Authorization to access PHI. [45 CFR §164.512(i)(1)(ii)]. See Section 16.4 for details.
20  Common Acronyms

AAHRPP: Association for Accreditation of Human Research Protection Programs
AE: Adverse Event
APS: Adult Protective Services
VPR: Vice President for Research
CC: Louisiana Children’s’ Code
CDS: Controlled Dangerous Substance
CFR: Code of Federal Regulations
CPS: Child Protective Services
CIP: Certified IRB Professional
CIRB: Central IRB for the National Cancer Institute
CITI: Collaborative Institute Training Initiative
CoC: Certificate of Confidentiality
COI: Conflict of Interest
Co-PI: Co-Principal Investigator
CRO: Contract Research Organization
CTA: Clinical Trial Agreement
CV: Curriculum Vitae
DHHS: U.S. Department of Health and Human Services
DOA: U.S. Department of Agriculture
DSMB: Data Safety Monitoring Board
EPA: U.S. Environmental Protection Agency
FDA: Food and Drug Administration
FWA: Federal Wide Assurance
GCP: Good Clinical Practice
HIPAA: Health Insurance Portability and Accountability Act
HRPO: Human Research Protection Office
HRPP: Human Research Protection Program
HUD: Humanitarian Use Device
ICH: International Conference on Harmonization
ICMJE: International Committee of Medical Journal Editors
IDE: Investigational Device Exemption
IIHI: Individually Identifiable Health Information
IND: Investigational New Drug Application
IO: Institutional Official
IRB: Institutional Review Board
LA R.S.: Louisiana Revised Statutes
MOU: Memorandum of Understanding
NCI: National Cancer Institute
NCT: National Clinical Trial
NIH: National Institutes of Health
OGC: Office of General Counsel
OHRP: Federal Office for Human Research Protections
OMB: Office of Management and Budget
ORA: Office of Research Administration
PHI: Protected Health Information
PI: Principal Investigator
QA/QI: Quality Assurance/Quality Improvement
RCO: Research Compliance Officer
SOPs: Standard Operating Policies
TUHC: Tulane University Hospital and Clinic
USC: U.S. Code
VA: Veterans Administration