Table of Contents
1 Mission ....................................................................................................................................................... 1
   1.1 Introduction ........................................................................................................................................ 1
   1.2 Ethical Principles: The Belmont Report ........................................................................................... 2
2 Definitions ............................................................................................................................................. 4
3 Institutional Authority ............................................................................................................................... 7
   3.1 Assurance of Compliance .............................................................................................................. 8
   3.2 Office for the Protection of Research Subjects (OPRS) ................................................................. 8
   3.3 Illinois Law ................................................................................................................................... 10
4 UIUC Institutional Review Board (IRB) ................................................................................................ 10
   4.1 Authority of the IRB .................................................................................................................... 10
   4.2 Jurisdiction of the IRB ................................................................................................................. 11
   4.3 OPRS and IRB Relationships ........................................................................................................ 11
   4.4 Roles and Responsibilities ........................................................................................................... 12
      4.4.1 Chairperson of the IRB ............................................................................................................... 12
      4.4.2 Vice Chair of the IRB ................................................................................................................... 13
      4.4.3 Subcommittees of the IRB .......................................................................................................... 13
   4.5 Resources for OPRS ..................................................................................................................... 14
   4.6 Conduct of Quality Assurance/Quality Improvement Activities for IRB and OPRS Operation ... 14
5 IRB Membership .................................................................................................................................. 15
   5.1 Composition of the IRB ............................................................................................................... 16
   5.2 Appointment of Members to the IRB ............................................................................................. 17
   5.3 Use of Consultants (Outside Reviewers) ....................................................................................... 18
   5.4 Duties of IRB Members ............................................................................................................... 19
7.4.1 Schedule of IRB Meetings ................................................................. 37
7.4.2 Quorum ......................................................................................... 37
7.4.3 Pre-Meeting Distribution of Documents ........................................ 38
7.4.4 Guests ......................................................................................... 38
7.4.5 Primary Reviewers ........................................................................ 38

7.5  Review Process .............................................................................. 39
7.5.1 OPRS Pre-review ......................................................................... 39
7.5.2 Materials Received by the OPRS .................................................. 39
7.5.3 IRB Member, Consultants or OPRS Staff Conflicts of Interest ...... 40
7.5.4 Possible IRB Actions Taken by Vote ............................................. 50
7.5.5 Determination of Risk ................................................................. 52
7.5.6 Period of Approval ................................................................. 52
7.5.7 Review More Often Than Annually ............................................ 54
7.5.8 Independent Verification Regarding Material Changes ............... 55
7.5.9 Consent Monitoring ................................................................. 56
7.5.10 Conflicts of Interest .............................................................. 56
7.5.11 Other Committee Approvals .................................................... 61
7.5.12 Reporting IRB Actions ............................................................ 61

7.6  Continuing Review of Active Protocols ........................................ 62
7.6.1 Continuing Review Process ....................................................... 63
7.6.2 Expedited Review of Continuing Review .................................... 64
7.6.3 Lapses in Continuing Review .................................................... 64

7.7  Modification of an Approved Protocol .......................................... 65
7.7.1 Expedited Review of Protocol Modifications ............................. 66
7.7.2 Full Board Review of Protocol Modifications

7.8 Unanticipated Problems/Events

7.8.1 Definitions

7.8.2 Reporting

7.8.3 IRB Review

7.9 Further Review/Approval of IRB Actions by Others within the Institution

7.10 Appeal of IRB Decisions

7.11 Sponsored Research Contracts

7.9 Research-Related Injury

7.10 Communication of Significant New Findings

7.11 Publications

8 Criteria for IRB Approval of Research

8.1 Risk/Benefit Assessment

8.1.1 Scientific Merit

8.1.2 Other Considerations

8.2 Selection of Subjects is Equitable

8.2.1 Recruitment of Subjects

8.3 Informed Consent

8.4 Data Safety Monitoring

8.5 Privacy and Confidentiality

8.5.1 Regulations

8.5.2 Privacy

8.5.3 Confidentiality and Anonymity
8.6 Vulnerable Populations ................................................................. 80

9 Informed Consent ................................................................. 80

9.1 Informed Consent Process ......................................................... 80

9.2 Basic Elements of Informed Consent ......................................... 81

9.3 Waiver or Alteration of Informed Consent ............................... 83

AND ................................................................. 84

9.4 Documentation of Informed Consent ......................................... 84

9.5 Waiver of Documentation of Informed Consent (Waiver of Signed Consent) .......................... 85

9.6 Review and Approval of the Informed Consent Form .................. 86

9.8 Surrogate Consent ................................................................. 88

9.9 Consent and Language Barriers .................................................. 89

10 Vulnerable Populations .............................................................. 90

10.1 Research Involving Children ................................................... 90

10.1.1 Definitions ........................................................................... 90

10.1.2 Allowable Categories .......................................................... 91

10.1.3 Parental Permission and Assent .......................................... 92

10.1.4 Additional Requirements for Conducting Research in the Schools ........................................... 97

Neonates .......................................................................................... 97

10.2.1 Definitions ........................................................................... 97

10.2.2 Research Involving Pregnant Women or Fetuses ................. 98

10.2.3 Research Involving Neonates ............................................ 100

10.2.4 Research Involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material ......... 101

10.2.5 Research Not Otherwise Approvable ..................................... 102

10.3 Research Involving Prisoners .................................................. 102
10.3.1 Applicability .............................................................................................................................. 103
10.3.2 Purpose ..................................................................................................................................... 103
10.3.3 Definitions .................................................................................................................................. 103
10.3.4 Composition of the IRB ............................................................................................................. 103
10.3.5 Additional Duties of the IRB ...................................................................................................... 104
10.3.6 Waiver for Epidemiology Research ........................................................................................ 105
Decision-Making Capacity ..................................................................................................................... 106
10.4.1 IRB Composition ...................................................................................................................... 106
10.4.2 Approval Criteria ....................................................................................................................... 106
10.4.3 Additional Concerns ................................................................................................................. 107
Termination of IRB Approval of Research .............................................................................................. 108
11.1 Complaints .................................................................................................................................... 108
11.2 Non-compliance ............................................................................................................................ 108
11.2.1 Definitions ................................................................................................................................. 108
11.2.2 Review of Allegations of Non-compliance ............................................................................. 109
11.2.3 Review of Findings of Non-Compliance ................................................................................ 110
11.2.4 Inquiry Procedures .................................................................................................................. 110
11.2.5 Final Review ............................................................................................................................ 111
11.2.6 Additional Actions .................................................................................................................... 112
11.3 Suspension or Termination ........................................................................................................... 113
11.4 Reporting ..................................................................................................................................... 114
Officials ................................................................................................................................................ 114
12.1 Procedures .................................................................................................................................... 114
13 Investigator Responsibilities ............................................................................................................. 116
13.1 Investigators ................................................................................................................................. 117
   Responsible Principal Investigators .............................................................................................. 117
   Student Investigators ....................................................................................................................... 117
   Research Team ............................................................................................................................... 118
13.2 Protocol Development .................................................................................................................. 118
13.3 Changes to Approved Research .................................................................................................... 119
13.4 Continuing Review after Protocol Approval .................................................................................. 119
13.5 Required Reports to the IRB ......................................................................................................... 120
   13.5.1 Unanticipated Problems ........................................................................................................ 120
   13.5.2 Complaints, Non-compliance and Protocol Deviations ......................................................... 121
   13.5.3 Progress Reports .................................................................................................................... 121
13.6 Investigator-Required Record Keeping ........................................................................................ 121
13.7 Investigators or Research Personnel Conflicts of Interest ............................................................ 121
   Research Team .................................................................................................................................. 122
   Orientation ........................................................................................................................................ 122
   Initial Education ................................................................................................................................ 123
   Waiver of Initial Education .............................................................................................................. 123
   Continuing Education and Recertification ...................................................................................... 124
   Additional Resources ......................................................................................................................... 124
13.9 Subject Recruitment ...................................................................................................................... 124
13.10 Payment to Subjects ................................................................................................................... 124
13.11 Investigator Concerns ................................................................................................................. 125
(HIPAA) ...................................................................................................................................................... 126
14.1 Historical Background ................................................................................................................... 126
<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.2</td>
<td>Effects of HIPAA on Research</td>
<td>126</td>
</tr>
<tr>
<td>14.3</td>
<td>Research under HIPAA</td>
<td>127</td>
</tr>
<tr>
<td>14.4</td>
<td>HIPAA and New Documentation Requirements</td>
<td>127</td>
</tr>
<tr>
<td>14.5</td>
<td>Patient Rights and Research</td>
<td>127</td>
</tr>
<tr>
<td>14.6</td>
<td>HIPAA and Existing Studies</td>
<td>127</td>
</tr>
<tr>
<td>14.7</td>
<td>Waivers to HIPAA Forms</td>
<td>127</td>
</tr>
<tr>
<td>15</td>
<td>Special Topics</td>
<td>128</td>
</tr>
<tr>
<td>15.1</td>
<td>Certificate of Confidentiality</td>
<td>128</td>
</tr>
<tr>
<td>15.1.1</td>
<td>Statutory Basis for Protection</td>
<td>128</td>
</tr>
<tr>
<td>15.1.2</td>
<td>Limitations</td>
<td>129</td>
</tr>
<tr>
<td>15.2</td>
<td>Mandatory Reporting</td>
<td>130</td>
</tr>
<tr>
<td>15.3</td>
<td>UIUC Students and Employees as Subjects</td>
<td>133</td>
</tr>
<tr>
<td>15.4</td>
<td>Departmental Subject Pool</td>
<td>134</td>
</tr>
<tr>
<td>15.4.1</td>
<td>Department of Psychology</td>
<td>134</td>
</tr>
<tr>
<td>15.4.2</td>
<td>Department of Educational Psychology</td>
<td>134</td>
</tr>
<tr>
<td>15.5</td>
<td>Student Research</td>
<td>135</td>
</tr>
<tr>
<td>15.5.1</td>
<td>Human Subjects Research and Course Projects</td>
<td>135</td>
</tr>
<tr>
<td>15.5.2</td>
<td>Independent Study, Theses and Dissertations</td>
<td>136</td>
</tr>
<tr>
<td>15.6</td>
<td>Oral History</td>
<td>137</td>
</tr>
<tr>
<td>15.7</td>
<td>Genetic Studies</td>
<td>138</td>
</tr>
<tr>
<td>15.7.1</td>
<td>Specimens</td>
<td>139</td>
</tr>
<tr>
<td>15.9</td>
<td>Transnational Research</td>
<td>142</td>
</tr>
<tr>
<td>15.10</td>
<td>Outreach to Research Participants</td>
<td>143</td>
</tr>
<tr>
<td>15.11</td>
<td>Drugs, Biologics or Medical Devices</td>
<td>143</td>
</tr>
</tbody>
</table>
16.1 Definitions ........................................................................................................................................ 144
16.2 Policy ............................................................................................................................................. 146
16.3 Procedures ..................................................................................................................................... 147
  16.3.1 Research Involving Medical Devices ....................................................................................... 147
  16.3.2 Research Involving Drugs and Biologic Products ................................................................. 151
16.4 Informed Consent ............................................................................................................................ 159
  16.4.1 Informed Consent – General Requirements ............................................................................. 159
  16.4.2 Basic Elements of Informed Consent for FDA Regulated Research ....................................... 159
  16.4.3 Documentation of Informed Consent ....................................................................................... 161
16.5 Emergency Use of a Test Article .................................................................................................... 164
16.6 Recruiting Study Subjects .............................................................................................................. 164
16.7 Data Retention and Subject Withdrawal in a Clinical Trial .......................................................... 166
17 Additional Requirements for Sponsored Research ............................................................................. 167
  17.1 Research Funded by the Department of Defense (DOD) ............................................................. 167
    17.1.1 Definitions ................................................................................................................................. 167
  17.2 Research Sponsored by the National Institute of Justice ............................................................ 173
    17.2.1 Privacy Certificate ...................................................................................................................... 173
    17.2.2 Confidentiality Statements ....................................................................................................... 174
    17.2.3 Research Conducted within the Bureau of Prisons................................................................. 174
  Educational Rights and Privacy Act (FERPA) ..................................................................................... 179
    17.3.1 Family Educational Rights and Privacy Act (FERPA) 34 CFR Part 99 ................................. 180
  17.4 Research Funded by the Environmental Protection Agency ...................................................... 184
    17.4.1 Definitions ................................................................................................................................. 184
    17.4.2 Research Involving Intentional Exposure of Any Human Subject ........................................ 185
17.4.3 Observational Research Involving Pregnant Women and Fetuses ........................................ 185
17.4.4 Observational Research of Children Not Involving Greater Than Minimal Risk ............... 185
17.4.5 Observational Research of Children Involving Greater than Minimal Risk ....................... 186
17.4.6 Final Review by EPA ........................................................................................................... 186
1 Mission

The University of Illinois at Urbana Champaign (UIUC) fosters a research environment that promotes the respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of the University. In the review and conduct of research, actions by UIUC 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), and will be performed in accordance with the Department of Health and Human Services (DHHS) policy, and regulations at 45 CFR 46 (also known as the “Common Rule”), and the Food and Drug Administration regulations at 21CFR50 and 21CFR 56. The actions of UIUC will also conform to all other applicable federal, state, and local laws and regulations.

To conduct this responsibility effectively, the University maintains an Institutional Review Board to review research protocols involving human subjects and to evaluate both risk and the procedures protecting subjects against risk. It is the function of the IRB to 1) determine and certify that all projects conform to the policies and procedures in this document and all applicable regulations regarding the health, welfare, safety, rights, and privileges of human subjects; and 2) assist the investigator(s) in complying with federal, state and local regulations.

1.1 Introduction

The UIUC Policies and Procedures for Human Research Protection Manual details the policies and procedures governing research with human subjects and the requirements for submitting research proposals for review by the UIUC Institutional Review Board. These policies and procedures apply to all research involving human subjects, regardless of sponsorship and performance site, if UIUC faculty, staff, students, or facilities are involved.

All institutional and non-institutional performance sites for this institution, domestic or foreign, will be obligated by this institution to conform to ethical principles which are at least equivalent to those of
UIUC, as cited in the previous section, or as may be determined by the Department of Health and Human Services (DHHS) Secretary.

1.2 Ethical Principles: The Belmont Report

It is the duty of the UIUC Office for the Protection of Research Subjects and the Institutional Review Board to review and make decisions on all protocols for research involving human subjects. The primary responsibility of the IRB is the protection of research subjects from undue risk and from deprivation of personal rights and dignity. This protection is best assured by the consideration of three principles, which are the touchstones of ethical research:

(1) that voluntary participation by the subjects, indicated by free and informed consent, is assured;

(2) that an appropriate balance exists between the potential benefits of the research to the subject or to society and the risks assumed by the subject; and

(3) that there are fair procedures and outcomes in the selection of research subjects.

These principles are summarized respectively as respect for persons, beneficence, and justice.

Respect for Persons: Voluntary Participation and Informed Consent.

One of the most important elements in any research involving human research subjects is the assurance of voluntary informed consent. Any person who is to be a research subject, whether designed for his/her own direct benefit or for the advancement of scientific knowledge in general, must understand as completely as possible what is to be done and what the potential risks and benefits of participation are. The person must give his/her consent freely, without pressure or inappropriate inducement. The IRB at UIUC strives to ensure voluntary informed consent of research subjects through careful review of the recruitment and consent process, including the consent form or information sheet to be used with subjects.

The informed consent process is extended to those studies in which the subjects are not able to give personal consent for themselves. Here the consent document is addressed to those who have been designated responsible for the research subject’s well being (e.g. parents of children). The IRB’s concern is to verify that the consent process and document are likely to assist these persons to make an
informed decision which is in the best interest of the research subject. Since the capacity for truly informed and voluntary participation in research varies widely among study populations, there may be ample understanding and manifest freedom from coercion at one extreme; at the other, there may be degrees of understanding and freedom that affect the consent of potential subjects. The IRB must exercise special care when considering subjects whose ability to give free and informed consent may be compromised in any way.

**Beneficence: The Risk-Benefit Ratio.**

The IRB is charged with deciding, for any proposed activity which falls under its jurisdiction, whether: “The risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept (those) risks” (Federal Register, May 30, 1974).

The assessment of the risk/benefit ratio is a complex task. There are risks of injury or discomfort to the individual that can be physical, psychological and/or social. There can be potential benefits to the individual, to a group to which the individual belongs, and/or to society. In reviewing applications, the IRB must carefully assess the types and degrees of both risks and benefits for a given subject population, as well as the investigator’s communication of these risks and benefits in the consent process and form. While the IRB is not charged with reviewing scientific design per se, it must sometimes do so in order to assess the risk/benefit ratio. If a study design does not seem adequate to attain the stated aim of the investigation, then no benefit can be anticipated from conducting the study, and there is no justification for placing any research subject at risk, however minimal. Thus the design of the study must be sound, and the nature and likelihood of all risks and benefits must be made clear in any application to the IRB.

**Justice: The Fair Selection of Research Subjects.**

Both the risks and the potential benefits of research should be spread fairly among potential individual research subjects and research subject groups. Study design and selection of subjects should avoid bias for or against particular social, racial, sexual, or ethnic groups.
Sharing Research Risks. The guiding principle in the ethical selection of research subject groups is that any risks of the research should fall upon the groups who might benefit from the research. If the results of a risky protocol might benefit the general population, it would be unethical to focus subject recruitment on vulnerable or disadvantaged groups (e.g. institutionalized people or prisoners; patients at free clinics primarily patronized by people unable to afford other medical care) simply because they are easily accessible or can be persuaded to participate. An undue share of research risks should not also burden groups already burdened by other factors. Instead, attempts should be made to include a fair sampling of the populations who might benefit from the study. When research involves persons whose autonomy is compromised, it is expected that the research bear some direct relationship to the conditions or circumstances of the research subject population. In addition, groups fully able to consider research risks and informed consent should be asked to face research risks before more vulnerable populations: investigational drugs are usually tested in adults before they are tested in children: certain investigational drugs and procedures may be tested in healthy volunteers before being tested in patients.

Sharing Research Benefits. In recent years, increasing attention has been paid to the rights of various groups to be included in research. As individuals and through advocacy groups, many patients have come to insist on having access to experimental treatments as these experimental treatments may potentially provide the best medical care available. In addition, researchers, ethicists and public officials have recognized that because many clinical trials focus primarily on white middle-class research subject groups, the results of some trials are of questionable value for members of other social, racial, sexual, and ethnic groups. As a result, both the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) now require that study design include as broad a range of research subjects as feasible and that data be analyzed to uncover responses that differ between groups. Where women of child-bearing potential, pregnant, and nursing women previously were routinely excluded from new drug trials, it is now required that whenever possible these women be asked to make their own choices after being fully informed of the risks of the research.

2 Definitions
**Human Subjects Research** – For the purposes of this policy “human subject research” is defined as an activity that meets the definition of “research” and involves “human subjects” as defined either by DHHS regulations or by FDA regulations (or other applicable funding agencies).

*Human Subject Research as defined by DHHS regulations:*

**Research** - a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition may be funded or unfunded, or may be conducted as a component of another program not usually considered research. For example, demonstration and service programs may include evaluation components, which constitute research activities under this definition.

**Systematic investigation** - an activity that involves a prospective research plan which incorporates data collection, both quantitative and qualitative, and data analysis to answer a research question. Investigations designed to develop or contribute to **generalizable knowledge** are those 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.

**Human subject** - a living individual about whom an investigator (whether professional or student) conducting research obtains:

1. Data through intervention or interaction with the individual, or
2. Identifiable private information.

**Intervention** includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

**Interaction** includes communication or interpersonal contact between investigator and subject.

**Private information** includes 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 (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.]  

**Human Subject Research as defined by FDA regulations:**  

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 Food and Drug Administration under Section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these Sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding non-clinical laboratory studies. An **experiment**, as defined in 21 CFR 312, includes any use of a drug other than the use of a marketed (approved) drug in the course of medical practice.  

**Human Subject** – an individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. In the case of a medical device, a human subject/participant also means a human on whose specimen an investigational device is used.  

**Human Subject Research as defined by the Department of Defense:**  

**Research Involving a Human Being as an Experimental Subject** - An activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction (32 CFR 219.102(f), reference (c)). Examples of interventions or interactions include, but are not limited to, a physical procedure, a drug, a manipulation of the subject or subject's environment, the withholding of an intervention that would have been undertaken if not for the research purpose. This definition does not include:  

- Activities carried out for purposes of diagnosis, treatment, or prevention of injury and disease in members of the Armed Forces and other mission essential personnel under Force Health Protection programs of the Department of Defense.  
- Authorized health and medical activities as part of the reasonable practice of medicine or other health professions.
• Monitoring for compliance of individuals and organizations with requirements applicable to military, civilian, or contractor personnel or to organizational units. This includes such activities as drug testing, occupational health and safety monitoring, and security clearance reviews.

Other Definitions:

IRB – an Institutional Review Board established in accord with and for the purposes expressed in this policy.

IRB approval – the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and federal requirements.

Minimal risk – the description 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.

RPI – Responsible Project Investigator - a non-visiting member of UIUC faculty or staff who takes ultimate responsibility for the protection of the subjects and the conduct of the human subjects research described on his or her IRB application.

Certification – the official notification by the institution to the supporting Department or Agency, in accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

3 Institutional Authority

The Chancellor of UIUC has designated the Vice Chancellor for Research as the Institutional Official (IO) for carrying out the University’s human research protections program.
The IO is responsible for ensuring that the UIUC Office for the Protection of Research Subjects (OPRS) has the resources and support necessary to comply with all institutional policies and with federal regulations and guidelines that govern human subjects research. The IO is legally authorized to represent UIUC. He/she is the signatory of the FWA and assumes the obligations of the FWA. The IO also has the authority to review and sign the Department of Defense Addendum for DoD sponsored research. The IO is the point of contact for correspondence addressing human research with the DHHS Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA). In the performance of these duties, the Institutional Official has the authority to delegate such activities as may be necessary in order to fulfill these duties.

The UIUC OPRS has jurisdiction over all human subject research (as defined above) conducted under the auspices of the institution. Research under the auspices of the institution includes research conducted at this institution, conducted by or under the direction of any employee or agent of this institution (including students) in connection with his or her institutional responsibilities, conducted by or under the direction of any employee or 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.

### 3.1 Assurance of Compliance

UIUC holds a Federalwide Assurance (FWA), FWA 00008584. The Federalwide Assurance (FWA) is an assurance of compliance with the federal regulations for the protection of human subjects in research that is federally funded. The FWA is also approved by OHRP for Federalwide use, which means that other departments and agencies that have adopted the Common Rule may rely upon the FWA for the research that they conduct or support.

In its FWA, UIUC has opted to apply only the Common Rule to all of its human subjects research regardless of the source of support. The subparts of 45 CFR 46 only apply to research funded by DHHS. See Section 10 for a more detailed discussion of the application of the subparts.

### 3.2 Office for the Protection of Research Subjects (OPRS)

The UIUC OPRS reports to the Associated Vice Chancellor (Compliance) for Research who reports to the
The Vice Chancellor of Research (who also serves as the Institutional Official and the Signatory Official on the Federalwide Assurance) and is supervised by the Director of the OPRS (Director). The Director has expert knowledge in regulatory issues regarding human subjects, and is the primary contact at UIUC for the Office for Human Research Protections, Department of Health and Human Services.

The Director of OPRS is a member of the staff of the Vice Chancellor for Research and is responsible for the overall operation of the OPRS. The Director meets regularly with the Associated Vice Chancellor (Compliance) for Research and communicates regularly with the Office of Sponsored Programs and other University business administrators as needed. Persons in these offices are not involved in the day-to-day operations of the IRB review or approval process and may not serve on the IRB in any capacity.

The Director responds regularly to faculty, student, and staff questions about human subjects research as well as organizes and documents the review process. The Director works closely with the Chairs of the IRB in the development of policy and procedures and she/he is a voting member of the IRB.

The OPRS is also staffed by one Human Subjects Coordinator, three Human Subjects Research Specialists, one Assistant Human Subject Research Specialist, one Office Support Specialist and multiple student workers as Office Support Staff.

The Human Subjects Coordinators, Human Subjects Research Specialists and the Office Support Staff are members of the staff of the Vice Chancellor for Research and provide administrative support, services and resources to the IRB and the UIUC research community. This includes organizing and reviewing submissions, consulting with the Director to identify issues in need of attention, and working with investigators to improve and clarify protocols (IRB applications) and related documentation.

The Office Support Specialist and Office Support Associate prepare IRB meeting packets, maintain IRB databases and correspondence, and assist the Director and academic staff in the OPRS.
3.3 Illinois Law
The University and the UIUC IRB rely on the counsel of the General Counsel of the University for the interpretation and application of Illinois law and the laws of any other jurisdiction where research is conducted as they apply to human subjects research.

4 UIUC Institutional Review Board (IRB)

The UIUC IRB is an administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of this institution. The Associate Vice Chancellor (Compliance) for Research, the Director of the OPRS, and the Chairs of the IRB will review the activity of the IRB on at least an annual basis and make a determination as to the appropriate number of IRBs that are needed for the institution.

4.1 Authority of the IRB
The IRB ensures that appropriate safeguards exist to protect the rights and welfare of research subjects [45 CFR 46.111]. In fulfilling these responsibilities, the IRB reviews all the research documents and activities that bear directly on the rights and welfare of the subjects of proposed research. The application or protocol, the consent/assent document(s), research equipment form, tests, surveys, questionnaires and similar measures, and recruitment documents are examples of documents that the IRB reviews.

Before any human subject is involved in research in relationship to this institution, the IRB will give proper consideration to:

1. The risks to the subjects;
2. The anticipated benefits to the subjects and others;
3. The importance of the knowledge that may reasonably be expected to result; and
4. The informed consent process to be employed.

The IRB has the authority to approve, require modifications to secure approval, and disapprove all research activities overseen and conducted by the organizations. The IRB has the authority to suspend,
place restrictions, or terminate approval of research activities that fall within its jurisdiction that are not being conducted in accordance with IRB requirements or that have been associated with serious harm to subjects. The IRB has the authority to observe or have a third party observe the consent process and/or the research if the IRB determines it to be indicated.

4.2 Jurisdiction of the IRB
The IRB jurisdiction extends to ALL research (funded and not funded) involving human subjects conducted at UIUC, as well as research conducted elsewhere by UIUC faculty, staff, and students, except research where the only involvement of human subjects is in one or more exempt categories (see 7.2.1 Categories of Research Permissible for Exemption).

If an IRB chair, IRB member, or OPRS staff person feels that the IRB has been unduly influenced by any party, they shall make a confidential report to the Vice Chancellor for Research and/or Chancellor, depending on the circumstances. The official receiving the report will conduct a thorough investigation and corrective action will be taken to prevent additional occurrences.

4.3 OPRS and IRB Relationships
The OPRS 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 OPRS 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 if it has been disapproved by the IRB.

Relationships with other institutions: UIUC may choose, on a case-by-case basis, to provide human research protection oversight for another institution. In order for the University to provide this oversight, a formal relationship must be established between the University and the other institution through a Cooperative Agreement, Authorization Agreement or a Memorandum of Understanding. This relationship must be formalized before the University will accept any human research proposals from the other institution.
In the conduct of cooperative research projects, UIUC acknowledges that each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with applicable federal regulations. When an authorization agreement exists, UIUC may enter into a joint review arrangement, rely on the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

- When UIUC relies on another IRB, the Director of the OPRS (or designee) will review the policies and procedures of the IRB to ensure that they meet UIUC standards. If the other IRB is part of an accredited Human Subject Protection Program (HRPP), then it will be assumed that the UIUC standards are being met.
- When UIUC reviews research conducted at another institution, the particular characteristics of each institution’s local research context must be considered, either (i) through knowledge of its local research context by the UIUC OPRS or (ii) through subsequent review by appropriate designated institutional officials, such as the Chairpersons and/or other IRB members.
- When UIUC is the coordinating center for a multi-center protocol, the OPRS will require the UIUC RPI to ensure that IRB approval has been obtained at each participating site prior to initiation of the research at that site. At the time of initial review, the OPRS will assess the procedures for dissemination of protocol information (e.g. unanticipated problems involving risks to participants or others, protocol modifications, interim findings) to all participating sites.
- For research sponsored by the Department of Defense, when conducting multi-site research, a formal agreement between organizations is required to specify the roles and responsibilities of each party.

4.4 Roles and Responsibilities

4.4.1 Chairperson of the IRB
The UIUC Institutional Official (Vice Chancellor for Research), in consultation and approval with the IRB members, and the Director of the OPRS, appoints a Chair and Vice Chair (as needed) of the IRB to serve for renewable three-year terms.
The IRB Chair should be a highly respected individual, from within 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 Chair. The IRB must be perceived to be fair, impartial and immune to pressure by the institution's administration, the investigators whose protocols are brought before it, and other professional and nonprofessional sources.

The IRB Chair may designate other IRB members to perform duties, as appropriate, for review, signature authority, and other IRB functions, e.g., the Vice Chair and Director of the OPRS.

The IRB Chair advises the Institutional Official and the Director of the OPRS about IRB member performance and competence.

4.4.2 Vice Chair of the IRB
The Vice Chair serves as the Chair of the IRB in the absence of the Chair and has the same qualifications, authority, and duties as Chair.

4.4.3 Subcommittees of the IRB
The Chair, in consultation with the Director of the OPRS, may designate one or more other IRB members, i.e. a subcommittee, to perform duties, as appropriate, for review, signature authority, and other IRB functions.

Duties of a subcommittee may include the following:

1. Serve as designees by the IRB Chair for the expedited review of new or continuing protocols, and/or modifications of continuing protocols. The 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.

2. Review and approve the revisions requiring only simple concurrence submitted by investigators for a protocol given provisional approval, i.e. “Approval Pending Revisions”, by the convened IRB.
3. **Conduct an inquiry.** A subcommittee is appointed consisting of IRB members, and nonmembers if appropriate, to conduct an inquiry into allegations of non-compliance. The subcommittee is given a charge by the IRB, which can include any or all of the following:
   a. Review of protocol(s) in question;
   b. 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;
   c. Interview of appropriate personnel if necessary;
   d. Preparation of either a written or oral report of the findings, which is presented to the full IRB at its next meeting;
   e. Recommend actions if appropriate.

4. **Conduct on-site review.** Determination of the review interval 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 an IRB subcommittee 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.

4.5 **Resources for OPRS**
The UIUC Institutional Official (Vice Chancellor for Research) provides resources to the IRB and OPRS, including adequate meeting and office space, and staff for conducting OPRS business. Office equipment and supplies, including technical support, file cabinets, computers, internet access, and copy machines, will be made available to the IRB and OPRS staff. The resources provided for the IRB and OPRS will be reviewed during the annual budget review process.

4.6 **Conduct of Quality Assurance/Quality Improvement Activities for IRB and OPRS Operation**
The OPRS staff will conduct audits of ongoing research when the IRB directs an audit be conducted or a complaint or allegation of non-compliance is received. In addition, the staff will conduct “for cause” and “not for cause” audits of research.
On an annual basis, the University will perform a review of the human research protections program. The goal of this review is to measure the effectiveness of the human protections program with respect to achieving and maintaining compliance. Some examples of such measures might include the number of lapses in research approval, changes in consent documents made prior to IRB approval, changes in key personnel made without submission of a Research amendment, etc. This will include a review of the following elements as described in written documents and as implemented in practice:

- Institutional and IRB policies and procedures for protecting human subjects;
- Organizational issues affecting systemic protections for human subjects;
- IRB documentation and records-keeping practices;
- Adequacy of IRB forms and templates;
- Standards and practices for initial and continuing IRB review;
- Standards and practices for obtaining and documenting informed consent;
- Standards and practices for monitoring compliance with IRB determinations;
- Standards and practices for monitoring unanticipated problems and adverse events.

The review may also include surveys of investigators or record audits for the purpose of assessing the overall human research protection program including the effectiveness of communication between the IRB and investigators; assessment of the training and education needs of investigators; to evaluate the effectiveness of the IRB website and resources; to solicit investigator satisfaction in general; to measure the submission to approval turnaround time; recordkeeping of reported incidents, etc.

All recommendations for improvement in the human research protections program will be considered by the IO and the Director. Changes in the program will be presented to the IRB for review prior to implementation.

5 IRB Membership
The Director of the OPRS in consultation with the IRB Chairs and the Vice Chancellor for Research identifies potential candidates for the IRB. Deans and department heads may also be requested to appoint faculty members to the IRB.

Appointments are made by the Vice Chancellor for Research for a three year period.

5.1 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 and expertise of its members, and the diversity of the members, including consideration of race, gender, and 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 (e.g., children, prisoners, pregnant women, or handicapped or mentally disabled persons), 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 5.3).

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, so long as no selection is made to the IRB on the basis of gender. 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. The IRB includes at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

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

9. The Director and staff of the UIUC OPRS may be voting members of the IRB.

5.2 Appointment of Members to the IRB
The IRB Chair(s), Vice Chair(s) and/or the Director of the OPRS, identifies a need for a new or replacement member, or alternate member. Nominated candidates’ names are sent to the OPRS. Department Chairs and others may forward nominations to the Institutional Official (Vice Chancellor for Research), to the OPRS, or to an IRB Chairperson.

For faculty members, the Director of the OPRS contacts the nominee. If there are no nominees, then appropriate Department Chairs or Program Directors will be contacted in writing by the Institutional Official, or the Director of the OPRS, concerning the vacancies and solicit nominees from the Department Chairs or Program Director.

The final decision in selecting a new member is made by the Institutional Official, the IRB Chair, and the Director of the OPRS. Individuals who are responsible for business development (e.g., Vice Chancellor for Research or Director of Office of Sponsored Programs) may not serve as members, alternates, or ex officio members on the IRB.

Appointments are made for a renewable three-year period of service. Any change in appointment, including reappointment or removal, requires written notification.

On an annual basis, generally in July, (or more frequently if necessary), the IRB Chair(s), Vice Chair(s) and the Director of the OPRS review the membership and composition of the IRB to determine if they
continue to meet regulatory and institutional requirements as described in section 5.1 above. This assessment is reported to the Institutional Official.

Alternate members:
The appointment and function of alternate members is the same as that for primary IRB members, and the alternate's expertise and perspective are comparable to those of the primary member. 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 primary member received or would have received.

The IRB roster identifies the primary member(s) for whom each alternate member may substitute. The alternate member will not be counted as a voting member unless the primary member is absent. The IRB minutes will document when an alternate member replaces a primary member.

5.3 Use of Consultants (Outside Reviewers)
When necessary, the IRB Chair or the Director of the OPRS may solicit individuals from the University or the community with competence in special areas to assist in the review of issues or protocols 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 by the Director or the Chair by reviewing the protocols. The OPRS will ensure that all relevant materials are provided to the outside reviewer. Only the IRB Chair, or one or more designated reviewers among members of the IRB, may carry out the review.

Written statements of consultants 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.

The Director of the OPRS reviews the conflicting interest policy for IRB members (section 7.5.3) with consultants and consultants must verbally confirm to the Director of the OPRS that they do not have a conflict of interest prior to review. Individuals who have a conflicting interest or whose spouse or family
members have a conflicting interest in the sponsor of the research will not be invited to provide consultation.

The consultant’s findings will be presented to the full board 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.

5.4 Duties of IRB Members
The agenda, submission materials, protocols, proposed informed consent forms and other appropriate documents are distributed to members prior to the convened meetings at which the research is scheduled to be discussed. Members review the materials at approximately one week before each meeting, in order to participate fully in the review of each proposed project. IRB members will treat the research proposals, protocols, and supporting data confidentially.

5.5 Attendance Requirements
Members should attend all meetings for which they are scheduled. If a member is unable to attend a scheduled meeting, they should inform the IRB Chair, Vice Chair, or an OPRS staff member. If the inability to attend will be prolonged, a request for an alternate to be assigned may be submitted to the Chair or the Director.

If an IRB member is to be absent for an extended period of time, such as for a sabbatical, he or she is instructed to notify the OPRS 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 5.3), the alternate can serve during the primary member’s absence, provided the OPRS has been notified in advance.

5.6 Training / Ongoing Education of Chair and IRB Members in Regulations, Procedures
A vital component of a comprehensive human research protection program is an education program for IRB Chair and the IRB members. UIUC is committed to providing training and an on-going educational process for IRB members and the staff of the OPRS, related to ethical concerns and regulatory and institutional requirements for the protection of human subjects.
Orientation

New IRB members, including alternate members, will meet with the IRB Chair and/or Director of the OPRS, OPRS staff and other IRB members as appropriate for an informal orientation session. At the session, the new member will be given an IRB Handbook (binder) that includes:

- Belmont Report;
- UIUC Policies and Procedures for the Protection of Human Subjects;
- Federal regulations relevant to the IRB

Initial Education

IRB members will complete the following web based training:

- UIUC Human Subjects Core CITI Training Module.
- FDA Regulated Research
- IRB Member Module – “What Every New IRB Member Needs to Know”

Continuing Education

To ensure that oversight of human research 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;
- Training workshops;
- Copies of appropriate publications;
- Identification and dissemination by the Director of new information that might have affected the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues to IRB members via email, mail, or during IRB meetings.
The Vice Chancellor for Research will provide support to send as many members of the IRB as possible to attend the annual PRIM&R conference or regional OHRP conferences on human research protections. The OPRS remains current with training and education requirements and opportunities by monitoring sources such as the OHRP listserv, DON HRPP, AAHRPP newsletter, IRB Advisor, the IRB Forum, NIH funding Opportunities and Notices, PRIM&R, Report on Research Compliance and other relevant sources. The OPRS Director is responsible for communicating initial and continuing training requirements to IRB members and the IO.

Completion of training is tracked by the OPRS staff in the OPRS Office. Members are encouraged to submit documentation of human research training received though sources other than the university (e.g., professional associations). IRB members who do not fulfill training requirements may have their responsibilities limited (e.g., may not be a designated reviewer) or may be removed from the IRB.

The OPRS Professional Staff is required to complete the entire CITI Course in the Protection of Human Research Subjects. Additionally, staff will be provided with opportunities to complete various trainings on topics related to human subjects research such as online webinars and national and regional conferences.

### 5.7 Liability Coverage for IRB Members
The University’s insurance coverage applies to employees and any other person authorized to act on behalf of the University or acts or omissions within the scope of their employment or authorized activity.

### 5.8 Review of IRB Member Performance
Performance of IRB members is evaluated on an ongoing basis by the OPRS Director and the IRB Chairs. Areas of performance include but are not limited to attendance and IRB meetings; meeting preparation; participation in IRB meetings; participation in ongoing education and training opportunities; knowledge and application of federal regulations and University policies; quality of reviews and availability for additional IRB duties.

On an annual basis (typically in July of each year) or more often as necessary, the Director and/or IRB chairs will inform the Institutional Official (or designee) about the performance of IRB members.
Members who cannot carry out their duties as IRB members, who do not act in accordance with the IRB Mission and policies, or do not contribute to the ethical and regulatory review of research with human subjects may be removed from the Board. An IRB member evaluation checklist has been developed to ensure each member is reviewed consistently.

5.9 Review of IRB Chairs Performance
The performance of IRB Chairs will be reviewed on an annual basis (or more frequently if necessary) by the Director of the OPRS in consultation with the Institutional Official (or designee). In addition to the performance areas listed for IRB Members in section 5.8, the Chairs are also evaluated, on their ability to manage IRB meetings, problem resolution skills, and ability to contribute to the development of institutional policies and procedures related to human research as deemed necessary. If the Chairs cannot carry out the duties of the Chair or do not act in accordance with the IRB Mission and policies, or do not contribute to the ethical and regulatory review of research with human subjects, the Chairs may be removed from the Board.

6 IRB Records
The OPRS must prepare and maintain adequate documentation of the IRB’s activities including: copies of all items reviewed, including, but not limited recruitment materials; scientific evaluations (if any) that accompany the proposals; approved consent documents including DHHS-approved sample consent documents; any proposed amendments and the IRB action on each amendment; reports of injuries to subjects and serious and unexpected adverse events; documentation of protocol violations; and documentation of non-compliance with applicable regulations. New findings provided to subjects must be maintained with the related research proposal and, when reviewed at an IRB meeting, must be documented in the minutes. Progress reports, continuing review documents and correspondence between the IRB and the investigator must also be retained.

Documentation of verified exemptions consists of the reviewer’s written concurrence that the activity described in the investigator’s request satisfies the conditions of the cited exemption category. This should be documented on the Exempt Determination Checklist.
IRB records for initial and continuing review by the expedited procedure must include: the specific permissible category; a description of action taken by the reviewer; and any determinations required by
the regulations and protocol-specific findings supporting those determinations. These will be noted on the OPRS Staff Review Checklists and the IRB Member Summary Checklists.

IRB records must document any determinations required by the regulations and protocol-specific findings supporting those determinations.

6.1 Minutes of an IRB Meeting
Proceedings of each IRB meeting must be written and available for review by the next regularly scheduled IRB meeting date. Once approved by the members at a subsequent IRB meeting, the minutes may not be altered by anyone including a higher authority.

Minutes of IRB meetings must contain sufficient detail to show:

- The basis for requiring changes in research;
- The basis for disapproving research;
- Justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document;
- The presence of a quorum throughout the meeting, including the presence of one member whose primary concern is in a non-scientific area. Minutes should reflect if a member leaves the room due to a conflict of interest;
- Attendance at the meetings including those members or alternate members who are participating through videoconference or teleconference and documentation that those attending through these mediums received all pertinent material prior to the meeting and were able to actively and equally participate in all discussions;
- Alternate members attending the meeting and for whom they are substituting;
- The initial attendance list which 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.
- Actions taken by the IRB including those involving full review. The IRB must use the minutes to notify IRB members of actions taken through expedited review and those studies that have been determined to be exempt from IRB review;
- Separate deliberations, actions, and votes for each protocol undergoing initial review, continuing review, or review of modifications by the convened IRB;
• Documentation that the research meets each of the required criteria [45 CFR 46.116(d)] along with protocol-specific information justifying why the IRB considers the research to meet each criterion 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 informed consent;

• Documentation that the research meets each of the required criteria [45 CFR 46.117(c)] along with protocol-specific information justifying why the IRB considers the research to meet each criterion when the requirements for written documentation of informed consent are waived;

• When approving research that involves populations covered by Subparts B, C, or D of 45 CFR 46, the minutes will document the IRB’s protocol-specific justifications and findings regarding the determinations stated in the Subparts or the IRB’s agreement with the findings and justifications as presented by the investigator on IRB forms.

• The vote on actions, including the number of members voting for, against, and abstaining from each vote;

• A note indicating that when an IRB member has a conflict of interest with the research under review, as defined by University policy (see Section 7.5.3.), relative to the proposal under consideration, the IRB member was not present during the deliberations or voting on that proposal;

• A written summary of the discussion of controverted issues and their resolution;

• Review of additional safeguards to protect vulnerable populations if entered as study subjects when this is not otherwise documented in IRB records;

• The frequency of continuing review of each proposal for initial and continuing review, as determined by the IRB;

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

As appropriate, minutes must also include information pertaining to:

• The approval period for initial and continuing review.

• Determinations required by the regulations, and protocol-specific findings justifying those determinations for:
- Research involving pregnant women, human fetuses and neonates.

### 6.2 Membership Rosters

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

1. **Name**
2. **Earned degrees**
3. **Affiliated, or non-affiliated** (neither the member nor an immediate family member of the member may be affiliated with the university) status
4. **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. Research experience includes training in research (e.g., doctoral degrees with a research-based thesis) and previous or current conduct of research
5. **Indications of experience**, such as board certifications or licenses sufficient to describe each member's chief anticipated contributions to IRB deliberations
6. **Representative capacities of each IRB member**: which IRB member is a prisoner representative (as required by Subpart C), 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
7. **Role on the IRB** (Chair, Co-Chair, etc.)
8. **Voting status** (i.e. Any ex officio members are non-voting members)
9. **Alternate status**, including the member they alternate with
10. **Relationship** (e.g., employment) between the individual IRB member and the organization

The OPRS must keep IRB membership list current. The Director of the OPRS (or designee) must promptly report changes in IRB membership to the Office for Human Research Protections within the Department of Health and Human Services.
6.3  Records Retention Requirements
The above detailed records must be stored securely in the OPRS and must be retained for at least 3 years. If records include HIPAA regulated research, they must be retained for at least 6 years.

Records pertaining to research must be stored securely in the OPRS and must be retained for at least three years after completion of the research. If a protocol is cancelled without subject enrollment, IRB records will be maintained for at least three years after cancellation.

After that time those records will be shredded or otherwise destroyed per the University of Illinois Records Disposal process. All records must be accessible for inspection and copying by authorized representatives of the OHRP, the FDA, sponsors, and other authorized entities at reasonable times and in a reasonable manner.

Records are maintained in locked file cabinets and/or locked offices within the OPRS and are available only to IRB members, OPRS and OVCR staff.

6.4  Written Procedures and Guidelines
The UIUC Policies and Procedures for Human Research Protection Manual details the policies and regulations governing research with human subjects and the requirements for submitting research proposals for review by the UIUC OPRS.

The policies and procedures present the most current information for reference by potential investigators and their staff; however, this is not a static document. The policies and procedures are annually reviewed and revised by the Director of the OPRS, the Institutional Review Board, and University counsel. The Vice Chancellor for Research will approve all revisions of the policies and procedures.

The Director of the OPRS will keep the University research community apprised of new information that may affect the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues on its website and through campus electronic mailing lists.
policies and procedures will be available on the UIUC OPRS website and copies will be available upon request.

7 IRB Review Process
These procedures and guidelines apply to all research involving human subjects, regardless of sponsorship and performance site, conducted under the auspices of UIUC.

7.1 Human Subjects Research Determination
The responsibility for the initial determination as to whether an activity constitutes human subjects research rests with the investigator. The investigator should make this determination based on the definitions of “human subject” and “research” in Section 2. Since the University will hold them responsible if the determination is not correct, investigators who are unsure are encouraged to request a confirmation that an activity does not constitute human subjects research from the OPRS Office. The request may be made verbally, by phone contact, by email or through formal written communication. All requests must include sufficient documentation of the activity to support the determination.

Within the OPRS Office, determination of human subjects research may be made by trained members of the OPRS Office staff or any member of the IRB. Determinations are made according to whether the activity meets the definition of “research” and involves “human subjects” using the DHHS Human Subjects Research Decision Charts. OPRS staff will respond in writing to formal requests for determination of human subjects research status. A copy of the submitted materials and determination correspondence will be kept on file in the OPRS Office.

7.2 Exempt Research
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. Studies that are FDA regulated may not qualify for an exemption. Exempt research is subject to institutional review and must be determined and approved by the IRB Chair, an IRB member, the Director of the OPRS Office, or trained staff member of the OPRS Office.

Exempt protocols will be closed and archived with the OPRS office 5 years after the initial approval date. If a researcher intends to continue their exempt research past 5 years, they can contact the OPRS office.
and request an extension of the protocol for an additional 5 year period. If there has been no attempt to contact the OPRS office before the end of the 5 year period, the protocol will be closed and archived. Once the protocol has been archived, any amendments to the protocol must be filed as new applications.

**Limitations on research subjects: Vulnerable Populations**

- **Children:** Exemption for research involving survey or interview procedures or observations of public behavior (category 2 for exemption) does NOT apply, except for research involving observations of public behavior when the investigator does not participate in the activities being observed. (See Section 10.1.1 for the definition of a child);
- **Prisoners, persons who are cognitively impaired, or persons who are economically or educationally disadvantaged:** exemptions do NOT apply. IRB review is required.

### 7.2.1 Categories of Research Permissible for Exemption

The categories of research permissible for Exemption are described on the OPRS Application for Exemption.

With the above limitations, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from IRB review, but require institutional review, at UIUC:

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.

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 or be damaging to the subjects' financial standing, employability, or reputation.

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; or
   b) Federal statute(s) require(s) without exception that the confidentiality of the personally 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. NOTE: In order to be eligible for this exemption, all of the materials have to exist at the time the research is proposed and must have been collected for purposes other than the proposed research.

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. Such projects must be conducted pursuant to specific federal statutory authority, there must be no statutory requirements for 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 U.S. Department of Agriculture.

NOTE: See Section 16 for further information on FDA regulated research.

7.2.2 How to Submit an Exemption Application

Investigators must submit the OPRS Application for Exemption that includes the following documentation:

1. a summary of the research 
2. a description of the research procedures 
3. a description of participants 
4. consent procedures 
5. plan for privacy and confidentiality 
6. plan for dissemination of findings 
7. a copy of the proposal if the research is externally funded 
8. expected date of completion 

The application must be signed and dated by the Responsible Principal Investigator.
Investigators will be given feedback, either by phone or email, as to the qualification of the application for exempt status. Once institutional review is completed, OPRS staff will send an email notifying the investigators of the final determination of the protocol.

7.2.3 Additional Protections
Although exempt research is not covered by the federal regulations, this research is not exempt from UIUC policies on responsible conduct of research or the ethical guidelines of the Belmont Report.

7.3 Expedited Review of Research
An IRB may use the expedited review procedure to review either or both of the following:

1. some or all of the research appearing on the list of research eligible for expedited review and found by the reviewer(s) to involve no more than minimal risk; and
2. minor changes in previously approved research during the period (of one year or less) for which approval is authorized.

A minor change is one which, in the judgment of the IRB reviewer, makes no substantial alteration in (i) the level of risks to subjects; (ii) the research design or methodology; (iii) the number of subjects enrolled in the research; (iv) the qualifications of the research team; or (v) the facilities available to support safe conduct of the research. Adding procedures that are not eligible for expedited review (See Section 7.4.1) would not be considered a minor change.

Under an expedited review procedure, the review may be carried out by the IRB Chair or by one or more reviewers designated by the Chair from among members of the IRB. 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.

The Chair (in consultation with the OPRS Director) will designate a list of IRB members eligible to conduct expedited review and the OPRS Office will select expedited reviewers from that list. IRB members eligible to conduct expedited review must have served on the IRB for at least three months.

When reviewing research under an expedited review procedure, the IRB Chair, or designated IRB member(s), will receive and review all documentation that would normally be submitted for a full-board review including the complete protocol, a Renewal Form summarizing the research since the previous
review (including modifications and unanticipated problems), notes from the pre-screening conducted by the OPRS Office staff, the current consent documentation and determine the regulatory criteria for use of such a review procedure by using the IRB Member Summary Checklist - Expedited Review.

The reviewer(s) conducting initial or continuing review complete the appropriate IRB Member Summary Review Checklist 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. Reviewers conducting an expedited review check the OPRS Staff Checklist for appropriateness of expedited category and concur by marking that category and signing on the IRB Member Checklist. When the IRB member disagrees with the staff’s determination, they provide the category and justification for the category.

In reviewing the research, the reviewers will follow the Review Procedures described in Section 7.5 and may exercise all of the authorities of the OPRS 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 or approval pending minor stipulations, or refer the protocol to the convened IRB meeting. If minor stipulations are required the OPRS staff will inform the investigator by email. If the stipulations are minor, the OPRS staff may determine if the investigator has sufficiently addressed the modifications. The reviewer also has the option to review the investigator’s responses directly to determine whether the stipulations have been sufficiently addressed. The reviewer may not disapprove the research. If the modifications are major or if the reviewer has other concerns, the protocol will be reviewed at the next convened IRB meeting.

In the event that expedited review is carried out by more than one IRB member and the expedited reviewers disagree, the OPRS Director and/or IRB Chair may make a final determination. Upon the discretion of the OPRS Director or IRB Chair the protocol will be submitted to the IRB for review.
7.3.1 Categories of Research Eligible for Expedited Review

The activities listed below should not be deemed to be of minimal risk simply because they are included on this list. 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. Note:

- The categories in this list apply regardless of the age of subjects, except as noted.
- The expedited review procedure may not be used 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.
- The expedited review procedure may not be used for classified research involving human subjects.
- The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

Research Categories one (1) through seven (7) pertain to both initial and continuing IRB review:

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met:
   
   (a) Research on drugs for which an investigational new drug application (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 product is not eligible for expedited review.)
   
   (b) Research on medical devices for which (i) an investigational device exemption application (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. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows: (a) from healthy, nonpregnant 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 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. [Children are defined in the DHHS regulations as "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." ][45 CFR 46.402(a)]

3. Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) hair and nail clippings in a nondisfiguring 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 subgingival 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 noninvasive 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 nonresearch 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 45 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 (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) 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.

[Note: for categories 8a and 8b the following applicability criteria apply: (1) the remaining
activities must be minimal risk, (2) if identification of the subjects or their responses will
reasonably place them at risk of criminal or civil liability or be damaging to the subjects’ financial
standing, employability, insurability, reputation, or be stigmatizing, reasonable and appropriate
protections will be implemented so that risks related to invasion of privacy and breach of
confidentiality are no greater than minimal, and (3) the research may not be classified research.
For category 8b the only applicability criterion is that the research may not be classified
research.

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
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.

[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.]
If a research protocol has been initially approved through a full-board review procedure, the continuing review may not be done by the expedited review procedure unless it falls within Category 8 or 9, above.

7.3.2 Informing the OPRS
All members of the IRB will be apprised of all expedited review approvals by means of the agenda for the next scheduled meeting under a section entitled "Staff Report." Copies of the expedited review approvals will be made available for any optional review at the request of any IRB member.

7.4  Convened IRB Meetings
Except when an exempt or expedited review procedure is used, the IRB must review proposed research at convened meetings (also known as Full-Board meetings) at which a quorum (see below) is present.

7.4.1 Schedule of IRB Meetings
In general the IRB meets once monthly. The schedule for the IRB may vary due to holidays or lack of quorum. Special meetings may be called at any time by the Chair or the Director of the OPRS.

7.4.2 Quorum
A quorum consists of a simple majority of the voting membership (or their designated alternates), including at least one member whose primary concern is in a non-scientific area. When the meeting agenda includes research protocols involving prisoners, a prisoner representative must also be present. It is also desirable for the presence of an un-affiliated member. The IRB Chair, with the assistance of the OPRS 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 meetings remain appropriately convened.

Votes may only occur when a quorum is present. The OPRS staff takes note of arrivals and departures of all members and notifies the chair if a quorum is not present. If a quorum is not maintained, the proposal must be tabled or the meeting must be terminated. All registered members present at a convened meeting have full voting rights, except in the case of a conflict of interest (see below). In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting.
A non-affiliated member represents the perspective of research participants. These members serve an essential and unique role to the IRB. While the presence of a non-affiliated member at the meeting is not mandated by DHHS or FDA to meet quorum, UIUC strives to ensure their attendance at every meeting.

It is strongly recommended that IRB members be physically present at the meeting. If physical presence is not possible, a member may be considered present if participating through teleconferencing or videoconferencing. In this case the member must have received all pertinent material prior to the meeting and must be able to participate actively and equally in all discussions.

7.4.3 Pre-Meeting Distribution of Documents
Place and time of meeting is set forth on the agenda cover sheet distributed to all IRB members. The agenda, with review assignments, and all protocols and supporting documentation to be reviewed are provided to all IRB members approximately one week prior to each meeting.

7.4.4 Guests
At the discretion of the OPRS, the Principal Investigator may be invited to the IRB meeting to answer questions about their proposed or ongoing research. The Principal Investigator may not be present for the discussion or vote on their research.

Other guests may be permitted to attend IRB meetings at the discretion of the IRB Chair and the Director of OPRS. Guests may not speak unless requested by the IRB and must sign a confidentiality agreement.

7.4.5 Primary Reviewers
The OPRS staff assigns a primary and secondary reviewer from the members of the IRB for all protocols requiring initial full review, continuing full review and for all protocols requiring full review of modifications to previously approved research. When making reviewer assignments, OPRS staff takes into consideration the vulnerable populations involved in the research and assign the protocol to at least one individual who has experience with this population. OPRS staff also takes into consideration the scientific or scholarly expertise required to review the research and assigns the protocol to at least one individual who has the appropriate scientific or scholarly expertise. If OPRS staff cannot identify a
primary reviewer with appropriate expertise, the IRB Chair or the Director of the OPRS will solicit consultants from the University or the community with competence in special areas to assist in the review of issues or protocols, which require appropriate scientific or scholarly expertise beyond or in addition to that available on the OPRS (see “Use of Consultants,” Section 5.3).

Before the meeting, each protocol application (including background information, project protocol, and informed consent) is reviewed by all IRB members.

At the meeting, the Primary and Secondary Reviewers present an overview of the goals, design, study procedures, safety procedures, and qualifications of the investigators and lead the IRB through the completion of the regulatory criteria for approval in the “Institutional Review Board - Protocol Review” checklist appropriate for the type of review (initial, continuing, amendment).

### 7.5 Review Process

#### 7.5.1 OPRS Pre-review
Applications are screened by the OPRS staff for completeness, using the “OPRS Staff Review Checklist,” and regulatory compliance prior to their placement on the agenda.

#### 7.5.2 Materials Received by the OPRS

Each IRB member receives the following documentation, as applicable:

1. Complete Protocol Application form;
2. Proposed Consent / Parental Permission / Assent Form(s);
3. Recruitment materials / subject information;
4. Data collection instruments (including all surveys and questionnaires);
5. The IRB Staff Review Checklist (pre-review);
6. Correspondence with the investigator.

At least one primary reviewer must receive and 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); the complete DHHS-approved protocol (when one exists); other funding proposal (and reviewer comments when appropriate).
If an IRB member requires additional information to complete the review they may contact the investigator directly or may contact OPRS to make the request of the investigator.

Protocol reviewers will use the IRB Member Summary Review Checklist as a guide to completing their review.

At the meeting, the Primary and Secondary Reviewer present an overview of the research and lead the IRB through the completion of the regulatory criteria (46.111) for approval in the IRB Member Summary Checklist.

When a protocol is reviewed by the expedited procedure, reviewers are provided and are expected to review all information that the convened IRB would have received. For expedited review protocols, any IRB member can also request to review the full protocol by contacting OPRS.

### 7.5.3 IRB Member, Consultants or OPRS Staff Conflicts of Interest

IRB members, consultants, or OPRS staff members will not participate in any IRB action taken in which the member has a conflict of interest, except to provide information requested by the IRB. IRB members are expected to self-identify conflicting interests. A primary reviewer or expedited reviewer with a conflict of interest must notify the OPRS staff who will re-assign the protocol.

Specifically, IRB members may not participate in any IRB action taken including:

- the initial and continuing review of any project at a convened meeting;
- the initial and continuing review of any project by expedited review;
- the review of unanticipated problems involving risks to participants or others;
- the review of non-compliance with the regulations or the requirements of the IRBs.

An IRB member, consultant, or OPRS staff member is automatically considered to have a conflict of interest when the member/consultant or the member’s or consultant’s family has any involvement in the design, conduct, or reporting of the research or a significant financial interest (SFI) in the sponsor, product, or service being tested that meets the following thresholds:
1. Remuneration received from an external entity at present or in the 12 months preceding the disclosure that when aggregated for the individual and family members the values totals or exceeds $5,000. The $5,000 threshold also applies to salary, royalties, and other payments aggregated for the individual and family members.

2. Ownership in a publicly-traded equity (plus any remuneration) when the value meets or exceeds $5,000.

3. Any level of ownership in a privately-held equity regardless of the dollar value.

4. Intellectual property rights (e.g., patents, trademarks, copyrights, licensing agreements, and royalties from such rights).

5. Any other relationships that might present a conflict of interest, such as fiduciary interests (paid or unpaid positions as director, officer, or other management role in a for-profit or not-for-profit entity sponsoring or related to the research) or interests in which compensation or the value of equity or property rights or the combination of interests might affect the outcome of the research.

6. Any gift regardless of value from a company or other entity that has an interest in the outcome of the human subjects research under review.

The following SFI are exempt (42 CFR 50.603) from the disclosure requirements:

i. salary, royalties or other remuneration paid by the University of Illinois; including intellectual property rights assigned to the University of Illinois and agreements to share royalties related to such rights;

ii. income from investment vehicles (mutual funds or retirement account that are not directly managed by the individual);

iii. income from seminars, lectures, or teaching engagements sponsored by a Federal, state, or local government agency, an Institution of higher education as defined by 20 U.S.C. 1001 (a); an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education; iv. income from service on advisory committees or review panels for a Federal, state, or local
government agency, an Institution of higher education as defined by 20 U.S.C. 1001 (a). (e.g., NIH review panel).

“Other Interest” includes but is not limited to:

1. Supervision of a project (i.e., an IRB member is the investigator’s Faculty Sponsor, or a situation exists in which any investigator must report to or is under the professional supervision of the IRB member);
2. Personal relationship with the investigator (IRB member has a family relationship or other close personal relationship with the investigator);
3. Other personal interests that may be a conflict of interest, such as if (a) the IRB member has an interest that he/she believes conflicts with the member’s ability to review a project objectively; or (b) the IRB member is in direct competition with the investigator for limited resources, funding, sponsorship, or research subjects, (c) the IRB member is considered a personal or professional adversary of the investigators, or (d) the IRB member is a subordinate to the investigator. For (b), (c), and (d), the IRB member should disclose the circumstances to the IRB Chair or OPRS director for a determination of whether a conflicting interest exists; and/or
4. Any other reason for which the member or consultant believes that he or she cannot provide an independent review.

Except when requested by the IRB to be present to provide information, IRB members will recuse themselves from the meeting room when the IRB reviews research in which they have a conflict of interest. The Chair will allow for board discussion once the conflicted member has recused him/herself. The absent member is not counted toward quorum and his/her absence during the discussion and vote on the protocol will be noted in the IRB meeting 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 Chair and/or OPRS Director.
*For purposes of this policy a family member means spouse or domestic partner, parents, siblings, and children.*

**Policy Section III. A. Persons Covered**

This Policy applies to all paid academic staff members, whether part time or full time employees of the university. The academic staff includes academic professionals, postdoctoral associates, and the faculty ranks of professor, associate professor, assistant professor (and all of the foregoing whose appointments contain such terms as "research," "adjunct," "visiting," or "clinical"), instructor, and lecturer. All covered persons are referred to herein as "academic staff members." For the purpose of this Policy, civil service staff, students, and medical residents (unless they are also employed as academic staff members) are not considered academic staff. Although civil service staff, students, and medical residents are not covered by this Policy, they are not exempted from making disclosures as required by federal or state laws and regulations or from making situation-specific disclosures as described in Section III.D.3.

**Policy Section IV. A. Disclosure of Non-University Activities**

Academic staff members must disclose external relationships that constitute actual or potential conflicts of interest, as well as all non-university income producing activities. These include but are not limited to all activities described in Section III.F as well as any other relationships, commitments, or activities on the part of academic staff members or their immediate family that might present or appear to present a conflict of commitment or interest with regard to their university appointment. These relationships may be of financial, fiduciary, or uncompensated nature, whether the external entity involved is for-profit or not-for-profit.

**Policy Section II. F. Examples of Potential or Actual Conflicts of Commitment or Interest Requiring Prior Approval**

The following activities represent examples of potential or actual conflicts of commitment or interest. The list is not inclusive and is intended to provide guidance. All examples are assumed to include both for-profit and not-for-profit entities.

1. Using university resources to conduct research that is sponsored by an entity in which the academic staff member or his/her immediate family member has a significant financial interest.

2. Serving in an executive or managerial capacity or holding significant financial interests in an entity doing business with the university.

3. Serving in an executive or managerial capacity or holding significant financial interests in an entity in one's field of research.
4. Serving on the board of directors or a major advisory committee of an entity that sponsors the academic staff member's research or provides gift funds for the use of the academic staff member or his/her department.

5. Conducting consulting or other non-university income producing activities involving university students or other university staff.

6. Utilizing university students or employees in the staff member's university activities supported by gift funds from an entity in which the academic staff member has a significant financial interest.

7. Utilizing university students or employees in the staff member's university research sponsored by an entity in which the academic staff member has a significant financial interest.

8. Conducting testing or clinical trials of products, devices, or services owned or controlled by an entity in which the academic staff member or a member of his/her immediate family has a significant financial interest.

9. Diverting research opportunities from the university to any external entity, (e.g., another academic institution, non-profit organization, federal laboratory, business, or consulting entity in which the staff member or a member of his/her immediate family has a significant financial interest, managerial, or executive role).

10. Owning an entity from which the university may seek to procure goods or services.

11. Influencing the university's decision to procure goods or services from an entity owned by one's immediate family member.

12. Submitting grant proposals or making sub award arrangements involving the purchase of goods or services from an entity in which an academic staff member or a member of his/her immediate family has a significant financial interest.

13. While acting in the context of his/her university duties, making professional referrals to an entity in which an academic staff member or a member of his/her immediate family has a significant financial interest.

14. Spending more than one day per seven-day-week (as defined in Section III.C.1), averaged over the contract period, on non-university income producing activities.

15. Other examples of activities for which prior approval is required include, but are not limited to: ownership and/or management of rental property, working at a retail entity, paid coaching, and providing or directing paid professional entertainment services.
Policy Section I. B. Definitions

"Immediate Family," for the purposes of this Policy, includes one’s spouse or domestic partner, parents, siblings, and children.

When a proposal is submitted to an organization that applies 42 CFR Part 50 Subpart F, the individuals named in the proposal are required to have completed the PHS FCOI training and disclosure at the time of submission. When a Just-in-Time request or Notice of Award arrives, the Office of Sponsored Program notifies the investigator and departmental business officer of the obligation to comply with 42 CFR Part 50 Subpart F and sends an “Investigator Identification and Verification of Training and Disclosure form” (Verification form, appendix B) to be completed. This form requires that all individuals who meet the definition of “investigator” as defined in the regulations must meet the training and disclosure requirements before funds can be spent.

Individuals who do not have a current disclosure on file, one filed within the academic year, are asked to complete the disclosure. Individuals who have not completed the training or who have not trained within 4 years are asked to complete the online training module.

Once the signed Verification form is received by the COI office, the disclosures for the listed investigators are reviewed to determine if there are SFI related to the specific research project.

In making this determination, the scope of work and aims of the research are reviewed. Consultation with the employee and his or her department head also occurs.

If a FCOI is identified, the appropriate management mechanisms are put in place and the required report to the funding agency is made.

Data on disclosures and training is maintained electronically. In accordance with University document retention and destruction policies, as approved by the State of Illinois, disclosures and related materials must be retained for at least six years after the year in which they were obtained. Additionally, no materials can be destroyed without the permission of the State. See Appendix E.
Financial Disclosure and Training Requirements for PHS Investigators
Financial Disclosure Processes for PHS Investigators
PHS Investigator Financial Interest Disclosure Form

PHS Investigator FCOI Training, slides from online training module, Appendix C.
We also hold in-person training sessions for lab groups.

PHS Travel Disclosure Video
PHS Travel Disclosure Web Form, Appendix D.

Investigator Identification and Verification of Training and Disclosure form, Appendix B

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42 CFR Part 50 Subpart F Materials

Financial Disclosure and Training Requirements for PHS Investigators
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PHS Travel Disclosure Video
PHS Travel Disclosure Web Form, Appendix D.

Investigator Identification and Verification of Training and Disclosure form, Appendix B

The Policy requires annual disclosure, Policy IV. Procedures A. Disclosure of Non-University Activities.
The PHS Investigator Disclosure form, Appendix A, notifies investigators of continuing obligation to update the disclosure within 30 days of acquiring an SFI. The disclosure requires that all SFI related to their institutional responsibilities be disclosed. Institutional responsibilities are defined as an Investigator's professional responsibilities on behalf of the institution, and as defined by the institution in its policy on financial conflicts of interest. This includes activities such as research or research
consultation, teaching, professional practice, institutional committee memberships, service on panels such as IRBs or data safety monitoring boards.

All non-University activity disclosure and PHS Investigator Disclosure forms are collected in the fall. Before PHS funding is released to be spent, all investigators must have a current disclosure on file. A website, phstraveldisclosure.research.illinois.edu (login required, web form posted in appendix D), is available to disclose sponsored or reimbursed travel related to investigators’ institutional responsibilities.

Once disclosures are sent to the COI office, those with nothing disclosed are filed and the completion date is recorded. Disclosures containing a disclosed interest are evaluated with respect to current research funded by organizations that follow 43 CFR Part 50 Subpart F. Consultation with the department head, employee, and committee, if in place, inform the determination of relatedness and whether the interest poses a conflict of interest. If a conflict of interest is identified, a conflict management committee is assembled by the department head. The committee, department head, COI administrator, and business contact meet with the conflicted investigator to review the SFI. The committee makes recommendations for management mechanisms which are included in the management plan. The plan is additionally reviewed and approved by a second level, usually the dean of the college, a delegate of the provost, and the executive associate vice chancellor for research.

Strategies to manage conflicts include:

• The relationship with the above-named external entity has been disclosed on the academic staff member’s RNUA (Report of Non-University Activities) and has been approved by the unit executive officer.

• The external entity will not have access to non-publicly available information until after the study has concluded and the results of the study have been publicly disseminated. The exception is if the external entity is the study sponsor. If the external entity is the study sponsor then the external entity may have access to non-publicly available information as a condition of the external entity’s contract with the University.

• No University resources will be utilized for the benefit of the above-named external entity without prior written agreement from the University.
• The researchers will employ an impartial review mechanism.

• The conflict will be disclosed in manuscripts, publications, presentations, etc. according to the norms of each publication venue.

• The conflict will be disclosed in writing to other research personnel (e.g., co-investigators, fellows, students).

• The conflicted person will not be involved in data collection or data entry.

• The conflicted person will not be involved in data analysis or the dataset will be given to an independent statistician for analysis.

• Non-conflicted individuals will be involved in study development (design, conduct, reporting).

• The study uses a blinded design (e.g., double- or triple-blind).

• The study includes oversight by an independent advisory board that will monitor the data (e.g. Data Safety Monitoring Board, Scientific Advisory Board).

• The conflict has been/will be disclosed to the IRB and the investigators agree to follow all IRB recommendations regarding conflict management.

• The COI will be disclosed to the sponsor of the research (and HHS/PHS sponsored research).

• The conflict will be disclosed to potential research participants in the informed consent process document or in the verbal informed consent process.

• The conflicted person will not solicit informed consent.

• The conflict will undergo increased frequency of continuing review and/or monitoring.

• Modification of the research plan.

• Change of research personnel or personnel responsibilities.

• Reduction or elimination of the financial interest. (e.g., sale of any equity interest)

• Severance of relationships that create financial conflicts of interest.

Policy III. B. Definitions
The definition of "significant financial interest" may vary. The definition to be used is based on either the federal or state definition and depends on whether the Public Health Service (U.S. Department of Health and Human Services; "PHS") regulation or the State Procurement Code is most clearly invoked in the situation
prompting the disclosure. The level of significance is determined by (as applicable) the dollar amount involved, the extent of ownership, and the degree of fiduciary responsibility held by the academic staff member or his/her family members. The unit requesting disclosure should carefully determine and specify the threshold for disclosure (percentage of equity ownership, dollar amount of financial interest, etc.) based on the applicable regulations. In the absence of other applicable regulations, financial interests greater than $5,000 will be considered significant. Any form requesting financial disclosure shall specify the threshold for disclosure.

Management plans
Management plans are reviewed on an annual basis and are updated whenever a change occurs. Management plans must be in place before entities in which the employee has an SFI can license or option intellectual property. Plans also must be in place before other agreements between University and the entity with which the employee has a conflict can be executed.

Policy IV. E. Sanctions for Violation of This Policy

Sanctions are warranted for failure to report potential conflicts or to abide by a management plan. The university has the right to impose sanctions consistent with the rights of academic staff members under the university Statutes and other applicable policies and practices. Severity of sanctions depends on the extent of the violations of the Policy. Inadvertent, unintentional, and minor breaches require lesser sanctions, whereas knowing, deliberate, and major violations demand the severest sanctions. Nothing in this Policy is intended to diminish or replace the procedural rights of academic staff, including the procedures for revocation of tenure contained in the Statutes.

7.5.4 Possible IRB Actions Taken by Vote

Approval - the study is approved as submitted.

Pending - the protocol and/or consent form require minor revisions, such as wording changes, with replacement language provided. The needed revisions are agreed upon at the meeting. These revisions are presented to the Principal Investigator for incorporation by simple concurrence. OPRS staff may
approve the study upon receipt and approval of the revisions without further action by the IRB. Note: 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 OPRS.

**Deferred for substantive issues (major stipulations)** regarding the protocol and/or consent form must be addressed. This action is taken if substantial modification or clarification is required, or insufficient information is provided to judge the protocol application adequately (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 RPI submitted by the convened IRB.

If the application is deferred the following will occur:

1. The OPRS informs the investigator in writing of the IRB's decision, questions and concerns.
2. The investigator's response is sent to the OPRS.
3. In order to receive approval for a deferred protocol, it must be submitted for full IRB review at a subsequent, convened meeting of the same IRB. The OPRS provides the IRB with the investigator’s response, the revised protocol and the previously submitted protocol. The item is placed on the agenda for a future meeting.
4. The protocol application is given full IRB review again.
5. The outcome of the IRB's deliberations is once again communicated to the investigator in writing.
6. The IRB's determination concerning the subsequent amended submission will be documented in the minutes of that meeting.

**Disapproved** - questions are of such significance that the IRB feels approval of the study is unwarranted. Approval of a previously disapproved protocol requires full IRB review. (If using the expedited review procedure the reviewer(s) may not disapprove the research. In such cases the protocol will be referred to the full board.)

**Approval in Principle** [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. One is if study procedures
are to be developed during the course of the research, but human subjects 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 as yet undeveloped recruitment, consent, and intervention materials. However, if the proposal is funded, the Principal Investigator 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.

**Appeals:** If the IRB makes a decision by expedited review that the investigator believes to be unduly restrictive, the investigator may appeal to the full IRB (7.10).

### 7.5.5 Determination of Risk
At the time of initial and continuing review, the IRB will make a determination regarding the risks associated with the research protocols. Risks associated with the research will be classified as either “minimal” or “greater than minimal” based on the “absolute” interpretation of minimal risk. The meeting minutes will reflect the Committee’s determination regarding risk levels.

### 7.5.6 Period of Approval
At the time of initial review and at continuing review, the IRB will make a determination regarding the frequency of review of the research protocols. All protocols will be reviewed by the IRB at intervals appropriate to the degree of risk. In some circumstances, a shorter review interval (e.g. biannually, quarterly, or after accrual of a specific number of participants) may be required. The meeting minutes will reflect the IRB’s determination regarding review frequency.

**Extended IRB Approval**

*Extended IRB Approval*
The UIUC Office for the Protection of Research Subjects (OPRS) allows flexibility in its application of human-subjects federal regulations to non-federally supported research.
Effective January 17, 2017, ORPS will implement procedures for granting IRB approval, for some protocols, for an extended period of up to 3 years.

**Studies Eligible for Extended IRB Approval**
- involves no more than minimal risk to participants (Expedited level of review as defined by 45 CFR 46.102),
- is not subject to federal oversight (as clarified below), and
- is not subject to UIUC’s Conflict of Interest review

**Studies not eligible for extended IRB approval**
- Research subject to Federal Oversight: Projects receiving federal support; implemented at the direction of federal agencies; or otherwise subject to federal oversight are excluded from this policy. *Examples of Federal oversight include:*
  - Federal sponsorship, directly or indirectly, including federal training and program project grants
  - Research directed or overseen by a federal agency that has signed on to the Common Rule, [link to: http://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html], including every agency within the Department of Health & Human Services
  - Student projects for which a faculty sponsor uses federal funding to support the project
  - Federal no-cost extensions
  - Studies subject to FDA oversight
  - Studies employing a Certificate of Confidentiality (issued by the NIH)
  - Studies for which the UIUC IRB is serving as the IRB of record for any institution which applies the federal standards to all research regardless of source of funding.
  - Research subject to Conflict of Interest review
- Studies involving greater than minimal risk
- Studies with contractual obligations or restrictions precluding eligibility to this policy (e.g., a non-federal sponsor or funder of the research which requires annual review).
- Studies involving data collection or data analysis on prisoners or those under court order

The UIUC IRB and OPRS reserves the right to make exceptions to this policy, and the conduct of any research project under this procedure will be at the IRB’s discretion (e.g., prior noncompliance).
If the UIUC IRB determines a study to be eligible for Extended IRB Approval, this determination will be referenced as part of the protocol approval letter. Studies granted an extended approval period will remain subject to all post-approval submission requirements. The Responsible Project Investigator (RPI) will remain responsible for submitting:

- modifications to the study (must receive IRB approval prior to implementation);
- reports of adverse events, protocol violation/incidents, and other safety information meeting OPRS reporting criteria;
- a continuing protocol application, at least 4-6 weeks prior to the study’s expiration date, if the study is still active

If there are any changes to the protocol that results in it being ineligible for extended IRB approval, the PI is responsible for notifying the IRB as an amendment immediately. The protocol will then be issued a modified expiration date accordingly.

### 7.5.7 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 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., institutionalized psychiatric patients, incarcerated minors); or
3. A history of serious or continuing non-compliance on the part of the principal investigator.

The following factors will also 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 Responsible Investigator and other members of the research team.
4. The specific experience of the Responsible Investigator and other members of the research team in conducting similar research.
5. The nature and frequency of adverse events observed in similar research at this and other institutions.
6. The novelty of the research making unanticipated adverse events more likely.
7. Any other factors that the IRB deems relevant.

In specifying an 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.

7.5.8 Independent Verification Regarding Material Changes
Protecting the rights and welfare of subjects sometimes requires that the OPRS verify independently, utilizing sources other than the investigator, information about various aspects of the study including but not limited to adverse event reporting, information in the scientific literature, reports of drug toxicity, drug approval status, and that no material changes occurred during the IRB-designated approval period.

The OPRS 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 occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources
2. Protocols conducted by Principal Investigators who have previously failed to comply with Federal regulations and/or the requirements or determinations of the IRB
3. Protocols randomly selected for internal audit
4. Whenever else the OPRS deems verification from outside sources is relevant
The following factors will also 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.
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 OPRS may prospectively require that such verification take place at predetermined intervals during the approval period, may retrospectively require such verification at the time of continuing review or may require such verification at any time during the approval period in light of new information.

### 7.5.9 Consent Monitoring

In reviewing the adequacy of informed consent procedures for proposed research, the OPRS 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.

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

### 7.5.10 Conflicts of Interest

Active participation by academic staff members in external activities that enhance their professional skills or constitute public service can be beneficial to the University as well as to the individual. Because such activities can lead to conflicts of commitment or interest with regard to one's University responsibilities, the need exists for a general framework against which the propriety and advisability of non-University activities can be measured and monitored.
The University of Illinois *Policy on Conflicts of Commitment and Interest* provides such a framework and identifies procedures for consultation and advice on conflicts of commitment or interest matters, for resolution of situations in which a conflict may exist, and for approval of exceptions when warranted. The *Policy* makes every effort to balance the integrity and interests of the University of Illinois with the integrity and interests of individual academic staff members. To that end, the *Policy* attempts not only to identify and eliminate or manage actual conflicts of commitment or interest but, whenever possible, to prevent even the appearance of conflicts. The *Policy* provides for remedies to manage conflicts constructively and for sanctions when the *Policy* is violated.

This *Policy* implements an Illinois law requiring all University faculty members to obtain prior written approval before engaging in remunerated private consulting or research for external persons or organizations. It also implements various policies set forth in the University Statutes and The General Rules Concerning University Organization and Procedure. Finally, the *Policy* was revised in 2012 to accommodate Department of Health and Human Service regulations designed to protect the objectivity of federally funded research.

**Managing Organizational Conflict of Interest at the University of Illinois at Urbana-Champaign**

**Organizational Structure**

The University of Illinois at Urbana-Champaign (UIUC) is a campus of the University of Illinois. The management of organizational conflicts of interest is aided by the structure of the University, in which the three campuses are overseen by a central administration, and intellectual property, equity interests and gifts are managed at the University level.

The chief officer of the UIUC campus is the Chancellor, who reports to the President of the University. Under the University’s *Policy on Conflicts of Commitment and Interest*, any significant financial interests of senior campus leadership (the Chancellor, or the Chancellor’s direct reports) are reviewed by the President, as first level of review for the Chancellor and second level of review for the Chancellor’s direct reports, and by the Board of Trustees as second level of review in the case of the Chancellor.

**Financial interests of senior administrators**

Senior administrators are subject to the University Policy on Conflicts of Commitment and Interest. Additionally, the individual campuses and the University Administration (UA) will each
conduct a coordinated annual disclosure and approval process for conflicts of commitment and interest. The president's annual disclosure will be reviewed and approved by the chair of the Governance, Personnel, and Ethics Committee of the Board of Trustees and by the chair of the Board of Trustees.

Policy III. D. Specific Responsibilities

1. Overall Responsibility
   The president or the president's designee has overall responsibility for all matters concerning conflicts of commitment or interest.

2. Responsibility for Information and Training
   The President will designate to the Vice President for Research the responsibility to identify a campus official that will be responsible for annually informing academic staff of this policy and implementing any associated training required by law. Academic staff members are responsible for complying with this policy and all training requirements. Training requirements may be imposed on other staff as required by federal and state law.

In addition to the University’s annual disclosure of outside activities and financial interests, the Illinois Government Ethics Act 5 ILCS 420/Art. 4A, mandates that members of the Board of Trustees of the University of Illinois, department heads, other administrative unit heads, those with responsibility for contracts of $5000 or more, and those who are principal investigators on grants complete a Statement of Economic Interests for review by the Illinois Secretary of State each year.

Management of University Financial Interests and Equity
Within the University administration, there is a University Investments Office, https://www.treasury.uillinois.edu/investments/, which manages the University’s financial investments, independent of the campus leadership.

The University generally does not retain equity in start-up companies. Once the company goes public or is purchased by another entity, the university sells its shares. This mitigates the potential organizational conflict of interest associated with University equity interest in faculty start-ups. There may be circumstances when the University retains some allocation of shares in the judgment that the market
value may increase over time. Those circumstances are determined and documented by OTM and the University's Treasury Operations.

The University’s Office of Technology Management is a unit within the University administration, and thus operates independently of the campus. Royalties from campus intellectual property are negotiated by this office, independently of the faculty and the campus leadership. The percentage of royalty return to the faculty is established by the University's General Rules. This arrangement mitigates potential conflict of interest when intellectual property created by campus faculty is being licensed to faculty start-up companies.

The campus policy, Licensing Intellectual Property Developed at the University of Illinois at Urbana-Champaign to Companies Affiliated with University Employees, http://www.cam.illinois.edu/iii/iii20.htm, requires that a conflict management plan be developed for any company licensing intellectual property from the University, in which an employee has a significant financial interest.

Management of Gifts in Support of Employee Research

The University of Illinois Foundation is an independent Illinois not-for-profit membership corporation registered with the state of Illinois, which is the official fundraising and private gift-receiving organization for the University and its three campuses. The Foundation has its own conflict of interest policy, http://www.uif.uillinois.edu/documents/COIResolution.pdf. Gifts to the University by employees or by employee start-up companies in support of their own programs are managed in accordance with policy Gifts by Employees in Support of Their Own Programs, https://www.obfs.uillinois.edu/gifts/fromemployees/.

Policy III. D. Basic Considerations. 2. Conflict of Interest.

Research agreements with external entities, especially entities with which academic staff members have a financial, managerial, or executive relationship, are of special concern. The terms and manner of executing such agreements must maintain basic academic values and promote the acquisition and dissemination of knowledge. Likewise, the educational experience of the university's students and postdoctoral fellows should not be diminished or impeded in any way; neither they nor other academic staff members should be diverted from their primary educational objectives.
Without prior written approval, it is improper for an academic staff member, having such a relationship, to divert to external entities or other institutions opportunities for research support that could have been obtained on behalf of the university.

**Management of Gifts to Employees**

The Illinois State Officials and Employees Ethics Act, 5 ILCS 430, establishes guidelines for ethical conduct by State employees. It sets strict limits on gifts that may be accepted by all state employees. University employees and those family members living in their household, are restricted from soliciting or accepting gifts of any sort from prohibited sources. Prohibited sources are people or businesses that do business or seek to do business with the University. This would include companies who engage in contracts with the University, such as research grants and contracts, or arrangements for clinical trials.

**7.5.10.1 Protocol-Specific Conflict Management**

The IRB application asks protocol-specific questions regarding conflict of interest for the investigators and key research personnel. Key research personnel are those individuals who: 1) recruit human subjects; 2) obtain consent from human subjects; 3) who collect data from human subjects; or 4) evaluate the response of human subjects.

If there is a financial conflict of interest, the investigator should submit an approved conflict of management plan. If the investigator does not provide the management plan, the IRB Office or IRB Chair may request the approved plan either from the investigator, unit head or from the Executive Associate Vice Chancellor for research who is an *ex officio* member of the Conflict of Interest Committee. If no approved conflict management plan exists, the IRB will request that the investigator(s) and key personnel work with their unit executive officer to develop one. The IRB protocol will not be reviewed until the management plan is in place.

As part of its review process, the IRB will review the conflict management plan (either at a convened meeting or by one or more reviewers as determined by the Chair) and make a determination as to whether the conflict adversely affects the protection of human subjects. If the IRB determines that the conflict does adversely affect human subjects, the management plan must be modified. The IRB has the
final authority to decide whether the management plan adequately protects the human subjects and the research can be approved.

If the conflict of interest status of an investigator changes during the course of a study, the individual is required to notify the Office for the Vice Chancellor for Research. The OPRS will review the change as a modification to the protocol.

At the time of continuing review, the investigator will be asked whether there has been any change in the conflict of interest status relating to the research. The IRB will review conflict of interest as part of its continuing review.

The review and disposition of the conflict management plans are documented in the IRB minutes or, in the case of expedited review, reported to the IRB monthly.

7.5.11 Other Committee Approvals
In the protocol application the investigator will be asked specific questions to determine if the research requires approval from other pertinent research compliance committees (Beckman Institute Biomedical Imaging Center, Institutional Biosafety Committee, etc.). If the investigator answers yes to any of the questions, then they will be requested to provide documentation of approval from the other committees. Final approval from the IRB will be contingent on receipt of the required documentation.

7.5.12 Reporting IRB Actions
All IRB actions are communicated to the Responsible Principal Investigator (RPI), or designated primary contact person for the protocol, in writing within ten (10) working days via a template letter prepared by the OPRS staff and signed by the OPRS Director or designee. For an approval, along with written notification of approval, a copy of the approved consent form containing the stamped approval with the dates of the approval and expiration on each sheet will be sent to the investigator. For a deferral, the notification will include the modifications required for approval along with the basis for requiring those modifications. For a disapproval, termination or suspension, the notification will include the basis for making that decision.

All letters to investigators are retained in the protocol files maintained by the OPRS.
The OPRS reports its findings and actions to the institution in the form of its minutes, which are distributed by OPRS staff to the UIUC Institutional Official and are stored permanently and securely in the Office for the Protection of Research Subjects.

### 7.6 Continuing Review of Active Protocols

The IRB will conduct a continuing review of ongoing research at intervals that are appropriate to the level of risk for each research protocol. 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 only to the analysis of private identifiable information.

At UIUC, 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 or OPRS 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 a specified approval expiration date. 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 OPRS staff 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 non-substantive 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 Chair gives final approval to the protocol or the OPRS staff conducts its final review of the study when the research was deferred for non-substantive issues.

The approval date and approval expiration date are clearly noted on all OPRS certifications sent to the RPI and must be strictly adhered to. Investigators should allow sufficient time for development and review of renewal submissions.
Review of a change in a protocol 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.

### 7.6.1 Continuing Review Process

To assist investigators, the OPRS staff will send out renewal notices to investigators two months and one month in advance of the expiration date; however, it is the investigator’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.

Investigators must submit the following for continuing review:

- the initial review application updated with any changes
- the current approved consent document
- any newly proposed consent document
- the protocol renewal form along with appropriate attachments related to changes in risk benefit ratio and changes that might affect the desire of subjects to continue participation

In conducting continuing review of research not eligible for expedited review, all IRB members are provided with and review all of the above material. The Primary Reviewer will review the complete protocol, including any modifications previously approved by the OPRS. At the meeting, the Primary and Secondary Reviewers lead the IRB through the completion of the regulatory criteria for approval in the “Institutional Review Board - Protocol Review/Continuing Review” checklist.

OPRS staff attend the convened meetings and bring the complete protocol files (including funding proposals when applicable) for each protocol on the agenda. The OPRS staff will retrieve any additional related materials that the IRB members request.
Review of currently approved or newly proposed consent documents must occur during the scheduled continuing review of research by the IRB, but informed consent documents should be reviewed whenever new information becomes available that would require modification of information in the informed consent document.

### 7.6.2 Expedited Review of Continuing Review

In conducting continuing review under expedited review, the IRB member receives all of the above material. The reviewer(s) complete the “Institutional Review Board - Protocol Review/Continuing Review” checklist to determine whether the research meets the criteria allowing continuing review using the expedited 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 categories (8) and (9) (see “Expedited Review Categories” Section 7.3.1). 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 IRB review would no longer be permitted for continuing review.

### 7.6.3 Lapses in Continuing Review

The OPRS and investigators must plan ahead to meet required continuing review dates. If the OPRS has not reviewed and approved a research study by the end of the approval period specified by the IRB, all research activities must stop, including recruitment (any and all 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.

**Note:** This may occur even if the investigator has provided the continuing information before the expiration date. Therefore, investigators must allow sufficient time for IRB review before the expiration date.
The IRB Chair reviews written requests of investigators to continue current subjects in research procedures. The IRB Chair determines which subjects, if any, may continue and what procedures may be performed if the Chair finds that stopping those research procedures will harm them. The IRB chair orally communicates the decision to investigators and also provides a written response. The IRB chair may not permit the enrollment of new subjects.

As a courtesy, the OPRS will send out renewal notices approximately two months before the studies expire. If no investigator response is received, a second notice will be sent approximately one month before the expiration date. However, it is ultimately the investigator's responsibility to initiate a renewal form, allowing sufficient time for the review and re-approval process to be completed before the current approval expires. Retrospective approval for work done after the expiration date cannot be granted.

An expiration letter (or email) will be sent to investigators by the last date of the approval period. Failure to submit continuing review information on time is non-compliance and will be handled according to the non-compliance policy (See Section 11.2). If the investigator does not supply the requested review information within 14 days after the expiration date, the file will be officially closed by OPRS. Once the file is closed the investigator will be required to submit a new application for IRB review and approval before continuing the research. OPRS will send the investigator a letter noting that the file has been closed. This letter will be copied to the funding agency and OSP (when research is funded).

7.7 Modification of an Approved Protocol
Investigators may wish to modify or amend their approved applications. Investigators must seek IRB approval before making any changes in approved research - even if the changes are planned for the period for which IRB approval has already been given - unless the change is necessary to eliminate an immediate hazard to the subject (in which case the IRB must then be notified as soon as possible).

Modifications may be approved if they are within the scope of what the IRB originally authorized. For example, if a researcher wishes to add a non-vulnerable population to an existing study, but not alter the study procedures or purpose, a modification request is usually appropriate. Likewise, modifying 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 revised application for human subjects approval.

Investigators must submit documentation to inform the IRB about the changes in the status of the study, including, but necessarily limited to:

- Completed IRB Research Amendment form;
- Revised Investigator’s protocol application or sponsor’s protocol (if applicable);
- Revised consent/parental permission/assent 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;
- Any other relevant documents provided by the investigator.

OPRS staff will determine whether the proposed changes may be approved through an expedited review process if the changes are minor, or whether the modification warrants full board review. The IRB member(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 full board review.

### 7.7.1 Expedited Review of Protocol 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 IRB Member(s) complete the “IRB Member Summary Checklist-Research Amendment Review” to determine whether the modifications meet the criteria allowing review using the expedited procedure, and if so, whether the research with the proposed modifications meets the regulatory criteria for approval.
7.7.2 Full Board 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 OPRS 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 IRB members are provided and review all documents provided by the investigator. At the meeting, the Primary Reviewer presents an overview of the modifications and leads the IRB through the completion of the regulatory criteria for approval.

When the IRB reviews modifications to previously approved research, the IRB considers 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.

7.8 Unanticipated Problems/Events
Federal regulations require organizations to have written policies and procedures to ensure the prompt reporting of unanticipated problems involving risks to subjects or others to the OPRS, appropriate institutional officials, and regulatory agencies. (NOTE: For simplicity, unanticipated problems involving risks to subjects or others will be referred to as “unanticipated problems” in this policy).

Not all unanticipated problems involve direct harm to subjects. Events can occur which are unexpected and result in new circumstances that increase the risk of harm to subjects without directly harming them. In addition, the event may have presented unanticipated risks to others (e.g., the sexual partners of the subjects, individuals the subject may come in contact with, family members, research personnel, etc.) in addition to the subjects. In each case, while the event may not have caused any detectable harm or adverse effect to subjects or others, they nevertheless represent unanticipated problems and should be promptly reported.

Events which direct harm to subjects are referred to as “Adverse Events”. Although adverse events occur most commonly in the context of biomedical research, adverse events can occur in the context of
social and behavioral research. Only unexpected adverse events that are related to the research need to be reported.

7.8.1 Definitions

Unanticipated Problem Involving Risks to Participants or Others (Unanticipated Problem): Any event or information that (1) was unforeseen and (2) indicates that the research procedures caused harm to participants or others or indicates that participants or others are at increased risk of harm.

Adverse event: Any physical, psychological or social harm to subjects during the course of research.

Unexpected: An event is “unexpected” when its specificity and severity are not accurately reflected in the informed consent document.

Related to the research: An event is “related to the research procedures” if in the opinion of the principal investigator, it was more likely than not to be caused by the research procedures or if it is more likely that not that the event affects the rights and welfare of current participants.

7.8.2 Reporting

Principal investigators must report the following types of events to the IRB as soon as possible:

1. Adverse events which in the opinion of the principal investigator are both unexpected and related

2. 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

3. 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

4. A breach of confidentiality

5. Incarceration of a participant in a protocol not approved to enroll prisoners.
6. Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant

7. Complaint of a participant when the complaint indicates unexpected risks or cannot be resolved by the research team

8. 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

9. Event that requires prompt reporting to the sponsor

10. Sponsor imposed suspension for risk

The IRB will accept other reports when the investigator is unsure whether the event should be reported. Principal investigators should report the above events using the Adverse Event form. Reports may be accepted by other means such as e-mail or phone.

Events that result in death, life-threatening experiences, hospitalization, or disability must be reported to the IRB within 24 hours after discovery.

All other unanticipated problems should be reported to the IRB within 5 working days.

Unanticipated problems are reported on at regular IRB meetings and noted whether or not they caused risk to the participants or to others. If the event has caused unexpected risk as a result of the research, the IRB will determine if procedures need to be changed and whether or not other participants should be contacted. This will be reported in the minutes.

7.8.3 IRB Review
Upon receipt of an Adverse Event form from a Principal Investigator, the OPRS staff checks the form for completeness. If any applicable sections of the Adverse Event form are incomplete or have been answered unsatisfactorily, the OPRS staff will contact the investigator 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 OPRS staff making the correction.
The OPRS staff submits the Adverse Event form and all supporting documents provided by the investigator to the IRB Chair or designee with the expertise to evaluate the event.

Based on the information received from the investigator and the evaluation by the designee member, the IRB Chair or Director may suspend research to ensure protection of the rights and welfare of participants. Suspension directives made by the IRB Chair or IRB Director must be reported to a meeting of the convened IRB.

If the IRB Chair or designee 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 IRB Chair or designee indicates on the form that the problem is not an unanticipated problem. The form is filed in the protocol record, the determination is communicated to the investigator and no further action is taken.

If the IRB Chair or designee considers that the problem is an unanticipated problem, but that the risk is no more than minimal, the chair or designee will review:

1. The currently approved protocol
2. The currently approved consent document
3. Previous reports of unanticipated problems involving risks to participants or others
4. The investigator’s brochure, if one exists.

After reviewing all of the materials, the chair or designee 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 chair or designee’s review will be recorded in the protocol file, communicated to the investigator, and reported to the OPRS, who will then comply with the reporting procedures detailed in Section 12.

All reported unanticipated problems where the risk is more than minimal will be reviewed at a convened IRB meeting. All IRB members are provided a copy of the Adverse Event form and supporting documents provided by the investigator. At least one IRB member is provided:
5. The currently approved protocol

6. The currently approved consent document

7. Previous reports of unanticipated problems involving risks to participants or others

8. The investigator’s brochure, if one exists.

If the IRB considers the event to not represent an unanticipated problem the results of the review are recorded in the protocol record, communicated to the investigator and no further action is taken.

If the IRB considers the event to represent an unanticipated problem, the IRB will consider the following actions:

1. Modification of the protocol

2. Modification of the information disclosed during the consent process

3. Providing additional information to current participants (This must be done whenever the information may relate to the participant’s willingness to continue participation)

4. Providing additional information to past participants

5. Requiring current participants to re-consent to participation

6. Alteration of the frequency of continuing review

7. Observation of the research or the consent process

8. Requiring additional training of the investigator

9. Notification of investigators at other sites

10. Termination or suspension of the research according to Section 11

11. Obtaining additional information

The results of the IRB review will be recorded in the protocol file, communicated to the investigator, and reported to the OPRS, who will then comply with the reporting procedures detailed in Section 12.
7.9 Further Review/Approval of IRB Actions by Others within the Institution

Research that has been approved by the IRB may be subject to further appropriate review and approval or disapproval by officials of the institution; however, those officials may not approve research if it has been not been approved by the IRB. [45 CFR 46.112] There are no required institutional reviews after the IRB grants approval, but the institution reserves the right to subject research reviewed by the IRB to further review.

7.10 Appeal of IRB Decisions

If a subcommittee of an IRB makes a decision that the investigator believes to be unduly restrictive on the proposed research, the investigator may appeal, in writing, for review by the convened appropriate IRB.

If the convened IRB makes a decision that the investigator believes to be unduly restrictive on the proposed research, the investigator should first discuss the matter with the Chair of the relevant IRB or the Director of the IRB Office, taking care to explain the reasons for believing that the proposed procedures are in compliance with University policy and with Federal regulations. If the issue cannot be resolved satisfactorily by negotiation, the investigator may appeal the decision of the IRB, in writing. The IRB will reconsider the appeal based upon the new information provided and will continue to re-review protocols as long as the investigator wishes to appeal.

7.11 Sponsored Research Contracts

All human subjects research must be reviewed and approved by the UIUC’s OPRS no matter the funding source, including gift, grant, or contract. Proposals for external funding, with an accompanying Proposal Transmittal Form (“PTF”), must also be sent to the UIUC Office of Sponsored Programs (“ODP”) for review and approval before the proposal can be submitted to the sponsor. The PTF gathers information about various compliance elements. The data from the PTF is recorded in UIeRA, the electronic research administration tool used by OSP. OSP Staff review the PTF at proposal and award stages to determine whether the project proposed for funding involves any compliance elements requiring review and/or approval by the applicable compliance office.

OSP provides the IRB with a monthly report noting all awards currently in process or recently executed which include a notation of use of human subjects or human anatomical materials. This report is
delivered to the IRB Director. This report allows the IRB to touch base with the faculty to ensure they have the appropriate protections in place, and thereby safeguard the research subjects.

As a general rule, the University complies with ICH GCP guidance (E6) only to the extent that the guidance is consistent with FDA and DHHS regulations. The ICH GCP (6) standards, which provide a unified standard to facilitate mutual acceptance of clinical data by regulatory authorities in the United States, European Union and Japan, have been adopted by the FDA as guidance only. The ICH GCP standards are not regulatory requirements in the United States.

However, where study sponsors require adherence to ICH GCP (E6) in its entirety, the University can agree to comply with the complete (E6) standards, provided that (i) the PI indicates in the protocol application that the PI understands the ICH GCP (E6) standards and is prepared to and will comply with the standards and (ii) OSP confirms that the funding agreement requires such compliance. OSP will notify OPRS when protocols must comply with ICH GCP (E6) standards. In those instances, the IRB will review the research protocol to identify aspects that may be inconsistent with ICH GCP (6). If the PI agrees to conduct an investigation in full compliance with the investigator obligations under ICH GCP (6), any compliance review conducted by the IRB will be performed against the ICH GCP (E6) requirements. The IRB will bring any issues of concern to the attention of the investigator, who may in turn ask for clarification from the sponsor.

Research-Related Injury

When the University enters in research agreements with sponsors the agreements will include language that addresses medical care for subjects who experience research-related injuries when appropriate. Such arrangements are determined before beginning the research and are communicated to the participants in the informed consent document. All efforts are made to ensure that the information in the contract is the same as in the informed consent document. When a research protocol is reviewed by the OPRS, the OPRS also reviews the funding agreement to ensure consistency.

Communication of Significant New Findings

During the course of the research investigators may learn of significant new findings (positive or adverse) that might affect the risks and benefits of the research as originally assessed by the investigator. Such findings might be based on adverse events, unanticipated problems or on reports
from data monitoring. As required by the informed consent document the investigator must inform subjects of such findings when they relate to the participant’s willingness to continue participation will be communicated to the subject.

In studies where the sponsor conducts research site monitoring visits or conducts monitoring activities remotely, the University will have a written agreement with the sponsor that the sponsor promptly reports to the University findings that could affect the safety of participants or influence the conduct of the study.

When the sponsor has the responsibility to conduct data and safety monitoring, the University will have a written agreement with the sponsor that addresses provisions for monitoring the data to ensure the safety of participants and for providing data and safety monitoring reports to the University.

When participant safety could be directly affected by study results after the study has ended, the University has a written agreement with the sponsor that the Investigator or the University will be notified of the results in order to consider informing participants.

Publications

For sponsored research, the University follows its policies on publication from findings for research funded by gifts, grants and contracts. If required by the sponsor, the University will provide the sponsor a short time period (usually 30 days) in which to review proposed publications, manuscripts, abstracts, and presentation materials, in order to determine whether proprietary or sponsor confidential information is disclosed.

8 Criteria for IRB Approval of Research

In order for the IRB to approve human subjects research it must determine that the following requirements are satisfied:

1. 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
2. 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 (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

3. Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes 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.

4. 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 §46.116.

5. Informed consent will be appropriately documented, in accordance with, and to the extent required by §46.117.

6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

8. 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.

### 8.1 Risk/Benefit Assessment

The goal of the assessment is to ensure that the risks to research subjects posed by participation in the research are justified by the anticipated benefits to the subjects or society. Toward that end, the IRB must:
1. 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.

2. Disapprove research in which the risks are judged unreasonable in relation to the anticipated benefits.

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

1. Identify the risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in research.
2. Determine whether the risks will be minimized to the extent possible.
3. Identify the probable benefits to be derived from the research.
4. Determine whether the risks are reasonable in relation to the benefits to subjects, if any, and assess the importance of the knowledge to be gained.
5. Ensure that potential subjects will be provided with an accurate and fair description of the risks or discomforts and the anticipated benefits.

8.1.1 Scientific Merit

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

• Risks to participants are minimized by using procedures consistent with sound research design and that do not unnecessarily expose participants to risk.
• Risks to participants are reasonable in relation to anticipated benefits, if any, to participants and the importance of the knowledge that may reasonably be expected to result.

For research that is funded externally or is internally funded (such as through Campus Research Board funds or the Critical Research Initiative) the IRB may take into account that the research has been or will be going through a peer review process. For internally funded research the reviewer’s comments will be forwarded upon request to the IRB member for review and will be retained along with the internal proposal in the file.
For departments that conduct scientific merit review, departmental scientific review is documented by the signature of the administrative official responsible for the investigator’s research unit specifically documenting that:

1. The research uses procedures consistent with sound research design
2. The research design is sound enough to yield the expected knowledge

In cases where the proposed research is not funded and there is no departmental scientific review, the IRB relies on the knowledge and disciplinary expertise of its members and alternates or consults with other researchers on or off campus for scientific merit review.

In all cases, the scientific or scholarly reviewer(s) must have the expertise to understand the background, aims, and methods of the research to answer the above questions and to draw on the discipline’s standards for conducting research.

### 8.1.2 Other Considerations

In assessing the benefits of the research, the IRB must also review:

1. The qualifications of the research team, including their technical and scientific expertise, as well as their knowledge and understanding of their obligation to protect the rights and welfare of research participants.
2. The adequacy of the resources necessary for human research protection, care of research participants, and safety during the conduct of the research.

### 8.2 Selection of Subjects is Equitable

The IRB will review the inclusion/exclusion criteria for the research to ensure equitable selection of subjects. In making this assessment the IRB takes into account the purposes of the research and the setting in which the research will be conducted, and is particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, fetuses, pregnant women, human in vitro fertilization, persons who are cognitively impaired, or persons who are economically or educationally disadvantaged (see section 8.6, Vulnerable Populations).
8.2.1 Recruitment of Subjects

The investigator will provide the IRB with all recruitment materials to be used in identifying participants including: the information contained in the advertisement; the mode of its communication; the final copy of printed advertisements; the final audio/video taped advertisements.

The IRB must approve any and all advertisements prior to posting and/or distribution. The IRB will review:

1. The information contained in the advertisement
2. The mode of its communication
3. The final copy of printed advertisements
4. The final audio/video taped advertisements

This information should be submitted to the IRB with the initial application or as an addendum to the protocol.

The IRB reviews the material to assure that the material is accurate and is not coercive or unduly optimistic, creating undue influence to the subject to participate, does not include exculpatory language, and does not promise “free treatment” when the intent is only to say participants will not be charged for taking part in the research.

Any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest such as:

- the name and contact information of the researcher or research facility
- the purpose of the research or the condition under study
- a summary of the criteria that will be used to determine eligibility for the study
- a brief list of benefits to participants, if any
- the time or other commitment required of the participants
- the location of the research and the person or office to contact for further information

Advertising should adequately describe the remuneration associated with services as a research subject, but shall not be displayed in such a manner as to emphasize payment as the primary incentive for involvement in the research.
8.3  Informed Consent
The IRB will ensure that 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. In addition, the Committee will ensure that informed 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 for detailed policies on informed consent.

8.4  Data Safety Monitoring
The IRB will review the data safety monitoring plan for protocols involving more than minimal risk during initial review and at continuing review.

8.5  Privacy and Confidentiality
The IRB will determine whether adequate procedures are in place to protect the privacy of subjects and to maintain the confidentiality of the data.

Definitions:

- Privacy – having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.
- Confidentiality – methods used to ensure that information obtained by researchers about their subjects is not improperly divulged.

Regulations

46.102(f) Human subject means a living individual about whom an investigator... conducting research obtains:

(1) data through intervention or interaction with the individual, or

(2) identifiable private information. Private information - information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).Identifiable information – information where the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
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’ information and the subjects expectations of privacy in the situation. Investigators must have appropriate authorization to access the subjects or the subjects’ information.

Confidentiality and Anonymity
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.

8.6 Vulnerable Populations
The IRB determine if appropriate additional safeguards are in place to protect the rights and welfare of subjects if they are likely to be members of a vulnerable population (e.g., persons with diminished autonomy). See Section 10 below for detailed policies on vulnerable populations.

9 Informed Consent
9.1 Informed Consent Process
No investigator may involve a human being as a 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 9.3 of this policy. In general, the IRB considers individuals who are unable to consent for their own clinical care to be unable to consent for research participation.

Investigators must obtain consent prior to entering a subject into a study and/or conducting any procedures required by the protocol, unless consent is waived by the IRB.

Consent must always be sought under circumstances that:
• provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate
• minimize the possibility of coercion or undue influence

The IRB will consider where the consent process will take place and the individual who will be obtaining consent (e.g. the investigator, collaborator, or qualified designee) in its determination regarding the appropriateness of the consent process. When the potential participant’s understanding of the research may be impaired due to the timing, location, or individuals participating in the proposed consent process, the IRB will require an alternative process.

The information that is given to the subject or the representative must be in a language that is understandable to the subject and/or the representative.

No informed consent, whether oral or written, may include exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject’s legal rights.

A person knowledgeable about the consenting process and the research (i.e., a member of the project’s research team) to be conducted must obtain the informed consent. If someone other than the investigator conducts the interview and obtains consent, the investigator needs to formally delegate this responsibility and the person so delegated must have received appropriate training to perform this activity.

9.2 Basic Elements of Informed Consent
Informed consent must be sought from each potential subject or the subject’s legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116. To ensure the basic and other elements, as applicable, are appropriately included in the consent form document, a consent form checklist has been developed. This form is used at the time of OPRS pre-review.

The basic elements of informed consent are:

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;
2. a description of any reasonably foreseeable risks or discomforts to the subject;

3. a description of any benefits to the subject or to others which may reasonably be expected from the research;

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

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

6. 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;

7. an explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject;

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. An explanation of whom to contact to voice concerns or complaints about the research.

10. 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; and in the event the subject wishes to talk to someone other than the research staff.

Additional elements of informed consent to be applied, as appropriate:

1. Anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s consent. The IRB and investigators also evaluate the subjects continued participation on an ongoing basis. Significant new findings obtained by the investigator or reported to the investigator (or to the University by the sponsor when the
sponsor is responsible for data and safety monitoring will be considered by the investigator in
determining whether a subject’s participation should be terminated

2. For transnational research, local contact information for whom the participant may call to
discuss problems, concerns, and ask questions regarding their role in the research study.

3. Any additional costs to the participant that might result from participation in the research

4. The consequences of a participant’s decision to withdraw from the research

5. Procedures for orderly termination of participation by the participant

6. A statement that if the participant was to become pregnant, the particular treatment or
procedure might involve risks to the embryo or fetus, which were currently unforeseeable

7. A statement that significant new findings developed during the course of the research which
might relate to the participant’s willingness to continue participation would be provided to the
participant

8. The approximate number of participants involved in the study.

9.3  Waiver or Alteration of Informed Consent
The IRB may approve a consent procedure which does not include, or which alters, some or all of the
elements of informed consent set forth above, or waive the requirement for informed consent provided
the IRB finds and documents that:

1. the research involves no more than minimal risk to the subjects

2. the waiver or alteration will not adversely affect the rights and welfare of the subjects

3. the research could not practicably be carried out without the waiver or alteration

4. whenever appropriate, the subjects must be provided with additional pertinent information
after participation

5. the research is not regulated by the FDA OR

1. 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:

   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

d) possible changes in methods or levels of payment for benefits or services under those programs

AND

2. the research could not practicably be carried out without the waiver or alteration.

For research funded by the Department of Defense, if the research subject meets the definition of “experimental subject,” a waiver of consent is prohibited unless a waiver is obtained from the Secretary of Defense. If the research subject does not meet the definition of “experimental subject,” the IRB may waive consent.

The investigator must submit the Waiver or Alteration of Informed Consent form with the original IRB application for review.

9.4 Documentation of Informed Consent
Informed consent must be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117:

3. Informed consent is documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent.

4. A copy of the signed and dated consent form must be given to the person signing the form.

5. The consent form may be either of the following:

   a) a written consent document that embodies the elements of informed consent may be read to the subject or the subject's legally authorized representative, but the subject or representative must be given adequate opportunity to read it before it is signed; or

   b) a short form written consent document stating that the elements of informed consent have been presented orally to the subject or the subject's legally authorized representative.

When the oral presentation of consent method (b. above) is used:
1. there must be a witness to the oral presentation (for participants who do not speak English, the witness is conversant in both English and the language of the participant.);
2. the IRB shall approve a written summary of what is to be signed by the subject or representative;
3. the witness must sign both the short form and a copy of the summary;
4. The participant or the participant’s legally authorized representative will sign the consent document.
5. the person actually obtaining consent must sign a copy of the summary;
6. a copy of the summary must be given to the subject or representative, in addition to a copy of the short form.

9.5 Waiver of Documentation of Informed Consent (Waiver of Signed Consent)
The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either that the:

1. The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality, and the research is not FDA-regulated. Note: 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.)
2. 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 and the research is not FDA-regulated. (Example: 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 investigator 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 investigator must also submit a Waiver of Documentation of Informed Consent with the IRB application for review.

### 9.6 Review and Approval of the Informed Consent Form

The IRB is responsible for the review and approval of the informed consent form prepared by the investigator. The wording on the informed consent form must contain all of the required elements and meet all other requirements as described in this section. If the wording of the informed consent has been initially prepared by an external entity other than a UIUC Principal Investigator, the IRB needs to ensure that the wording of the consent meets all the requirements of, or has been reviewed by, the appropriate University committees and subcommittees.

IRB approval of the consent form is documented by a certification stamp indicating the expiration date. If the consent form is amended during the protocol approval period, the form still must state the original expiration date.

The investigator will obtain the legally effective informed consent of the participant or the participant’s legally authorized representative. OPRS staff and IRB board members utilize reviewer checklists that include an element designed to prompt consideration of this issue. Particular emphasis is placed on this issue to ensure that the assent of any individual under age 18 is accompanied by some form of consent from the child’s parent(s) or guardian(s). This is also a focus of concern for any situation where the participant (even if an adult age 18 or over) experiences a cognitive impairment that makes it essential that a guardian serve as a witness to a signature or that a proxy for that individual provides consent.

The circumstances of the consent process provide the prospective participant or the legally authorized representative sufficient opportunity to consider whether to participate. OPRS staff and IRB board members utilize reviewer checklists that include an element designed to prompt consideration of this issue. The consent process should be carefully detailed on the IRB-1 application. The information provided should detail how each potential participant will have an opportunity to ask questions prior to
any signature of consent or other form of agreement when a waiver/alteration of signed consent is sought.

The circumstances of the consent process minimize the possibility of coercion or undue influence. In particular, the IRB must determine that there is no undue coercion or undue influence in relation to the following situations:

1. that there is no monetary gift, compensation or remuneration that is out of proportion to the amount of time/effort that participants would expend during their involvement in the research. This must be carefully assessed to ensure that remuneration might make participation in the study difficult for them to reject (even if the individual didn’t really want to volunteer) in order to receive the compensation. This would be a particular concern when remuneration is being offered to individuals from vulnerable populations who have minimal financial resources.

2. when the investigators are also the course instructors of University of Illinois students who are being recruited to participate in the investigator’s research. In these cases there might be perceived coercion on the student’s part that influences them to participate to please the professor and/or avoid retribution related to grading. The same issue would hold true whenever a University of Illinois researcher is recruiting for their studies other UIUC faculty, staff, or students who are being supervised by that researcher in any manner.

When the target population involves a significant number of participants (at least 5% of potential participants) for whom English is not the primary language, efforts shall be made by the investigator to provide translation services and to offer translated consent documents whenever necessary.

The information being communicated to the participant or the representative during the consent process may not include exculpatory language through which the participant or the legally authorized representative was made to waive or appear to waive any of the participant’s legal rights. There are reviewer checklist items that prompt both OPRS staff and IRB board members to review the consent document carefully in this regard to make sure that no statement appears on the consent document that waives or appears to waive a participant’s legal rights.
9.7  Parental Permission and Assent  
See Section 10.1.1 for policies on parental permission and assent in research involving children.

9.8  Surrogate Consent  
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.

Unless waived by the IRB, informed consent must be obtained directly from the individual subject. Under appropriate conditions, investigators also may obtain informed consent from a legally authorized representative of a subject (surrogate consent).

**Definition:** Legally authorized representative means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedure(s) involved in the research [45 CFR 46.102(c)].

The General Counsel of the University has determined that, in Illinois, the following meet the definition legally authorized representative and, thus, can give surrogate consent:

- A court appointed guardian of the person.
- A health care agent appointed by the person in a Durable Power of Attorney for Health Care (DPAHC) that specifies that the individual also has the power to make decisions of entry into research.

Investigators should consult with the General Counsel of the University when conducting research outside of Illinois to determine what the requirements for a legally authorized representative in the jurisdiction in which the research is taking place.

Such consent may be requested and accepted only when the prospective research participant is incompetent or has an impaired decision-making capacity, as determined and documented in the person’s medical record in a signed and dated progress note. The determination must be made in accordance with the following requirements:
1. The practitioner 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.

2. Consultation with a psychiatrist or licensed psychologist must be obtained when the determination that the prospective research subject lacks decision-making capacity is based on a diagnosis of mental illness.

The IRB will require investigators to conduct a competency assessment whenever there is a possibility of either impaired mental status or decision-making capacity in prospective subjects. The IRB will evaluate whether the proposed plan to assess capacity to consent is adequate.

If feasible, the investigator must explain the proposed research to the prospective research subject even when the surrogate gives consent. Under no circumstances may a subject be forced or coerced to participate in a research study. The IRB will evaluate whether a) the assent of the subjects is required, and b) whether plan for obtaining assent is adequate.

9.9 Consent and Language Barriers
Researchers should prepare both English language and translated consent forms for proposals that include non-English-speaking subjects. An explanation of the translations and evidence of the comparability of the English and non-English consent forms is requested. Researchers must complete the Certificate of Translation document. The IRB may consult with language experts or require a "backtranslation" into English. The translation should provide documentation to verify the accuracy of the translation and back-translation.

If a non-English-speaking subject is enrolled unexpectedly, researchers may rely on an oral translation of the English language consent form, but should take extra care in the informed consent process to ensure that the subject has understood the project. A statement in the research records (and on the English language consent form) should indicate that the translation took place, identify the translator, and document the translator's belief that the subject understands the study and the consent process. If the subject is a patient, a note about the translation should be made in the patient's research records as well. Researchers should try to provide a written translation of the vital emergency contact information.
Sometimes a subject understands English but does not read or write English. Again, an impartial witness should document that the subject understood the research and the consent process and consented to participate.

10 Vulnerable Populations

10.1 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, which applies to DHHS-funded research and Title 21, Part 50, Subpart D, which applies to FDA research.

10.1.1 Definitions

Child - In Illinois a child is defined as an individual who has not attained 18 years of age.

*NOTE:* For research conducted in jurisdictions other than Illinois, the research must comply with the laws regarding the legal age of consent in all relevant jurisdictions. The General Counsel of the University’s Office will provide assistance with regard to the laws in other jurisdictions.

Guardian – In Illinois a “Guardian” of a minor means the duty and authority to act in the best interests of the minor, subject to residual parental rights and responsibilities, to make important decisions in matters having a permanent effect on the life and development of the minor, and to be concerned with his or her general welfare.

*NOTE:* For research conducted in jurisdictions other than Illinois, the research must comply with the laws regarding guardianship in all relevant jurisdictions. The General Counsel of the University’s Office will provide assistance with regard to the laws in other jurisdictions.

Assent - a child's affirmative agreement to participate in research. Mere failure to object, absent affirmative agreement, should not be construed as assent.

Permission - the agreement of parent(s) or legal guardian(s) to the participation of their child or ward in research.

Parent - a child's biological or adoptive parent.
10.1.2 Allowable Categories
Research on children must be reviewed and categorized by the IRB into one of the following groups:

1. Research 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). [45 CFR 46.404][21 CFR 50.51]
   • The IRB may find that the permission of one parent is sufficient.

2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subject. [45 CFR 46.405] [21 CFR 50.52]
   • The risk is justified by the anticipated benefit to the subjects;
   • The IRB may find that the permission of one parent is sufficient;
   • Requires assent of the child.

3. Research involving greater than minimal risk and no reasonable prospect of direct benefit to the individual subject, but likely to yield generalizable knowledge about the subject’s disorder or condition. [45 CFR 46.406] [21 CFR 50.53]
   • 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 participants’ disorder or condition which is of vital importance for the understanding or amelioration of the participants’ disorder or condition.
   • Permission of either both parents, or legal guardian, is required unless one parent is deceased, unknown, incompetent, or not reasonably available; or only one parent has legal responsibility for the care and custody of the child;
   • Requires assent of the child.
Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of children. [45 CFR 46.407] [21 CFR 50.54]

- DHHS-funded research in this category must be approved by the Secretary of Health and Human Services, and requires consent of either both parents, or legal guardian. If the IRB determines that the research falls in this category, the research will be sent to OHRP for DHHS review.

- For non-federally-funded research, IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB may approve the research based on either:
  
  a) That the research in fact satisfies the conditions of the previous categories, as applicable; or
  
  b) The following:
    
    i. 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;
    
    ii. The research will be conducted in accord with sound ethical principles; and
    
    iii. Informed consent will be obtained in accord with the provisions for informed consent and other applicable sections of this manual.

10.1.3 Parental Permission and Assent

10.1.3.1 Parental Permission

In accordance with 45 CFR 46.408(b) and 21 CFR 50.55(a), the IRB must determine that adequate provisions have been made for soliciting the permission of each child’s parents or guardians.

Permission from both parents is required for all research to be conducted with children unless: one parent is deceased, unknown, incompetent, or not reasonably available; or when only one parent has legal responsibility for the care and custody of the child; or the research falls under 1 and 2 above and the IRB has determined that the permission of one parent is sufficient.
Parents or guardians must be provided with the basic elements of consent as stated in 45CFR 46.116(a)(1-8) and 21 CFR 50.25(a-d) and any additional elements the IRB deems necessary. The IRB may find that the permission of one parent is sufficient for research to be conducted under 45 CFR 46.404, 45 CFR 46.405, or 21 CFR 50.55(e)(1). The IRB’s determination of whether consent must be obtained from one or both parents will be documented in the consent checklist when a protocol receives expedited review, and in meeting minutes when reviewed by the convened committee.

Consent from both parents is required for research to be conducted under 45 CFR 46.406, 45 CFR 46.407, and 21 CFR 50.55(e)(2) unless:

- One parent is deceased, unknown, incompetent, or not reasonably available; or
- When only one parent has legal responsibility for the care and custody of the child.

The IRB may waive the requirement for obtaining consent from a parent or legal guardian if:

- The research meets the provisions for waiver in 45 CFR 46.116(d)(1-4) and if the IRB determines that the research protocol is designed for conditions or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children).
- 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 law. 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.

The IRB may not waive parental permission if the research is subject to FDA regulation.

10.1.3.2 Assent from Children

Because “assent” means a child’s affirmative agreement to participate in research, [45 CFR 46.402(b)] and [21 CFR 50.3(n)], 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 UIUC IRB has the discretion to judge children’s
capacity to assent for all of the children to be involved in a proposed research activity, or on an individual basis.

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 (for example, 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 in section 9 above.

The Assent Form
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 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's okay 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.

IRB Determination of Assent Requirement
Taking the factors above into consideration, when approving research involving children the IRB must determine and document that assent is a requirement of:

- All children in the research;
- Some children in the research; or
- None of the children in the research.

95 | UIUC Office for the Protection of Research Subjects, Policy Manual, 09.08.2017
When the IRB determines that assent is not a requirement of some children the IRB shall document which children are not required to assent and indicate one or more of the following reasons:

1. The children are not capable of providing assent based on their current age, maturity, or psychological state;
2. The capability of the children is so limited that they cannot reasonably be consulted;
3. 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 child and is available only in the context of the research; or
4. The assent can be waived using the criteria for waiver of the consent process.

**Documentation of Assent**

The IRB has the discretion to determine the appropriate manner, if any, of documenting child assent. Based on such considerations as the child’s age, maturity, and degree of literacy, the IRB should decide what form of documentation, if any, is most appropriate.

**10.1.3.3 Children who are Wards**

Children who are wards of the State or any other agency, institution, or entity can be included in research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition, only if such research is: related to their status as wards; or 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 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.
10.1.4 Additional Requirements for Conducting Research in the Schools

Additional requirements for research supported by the Department of Education or otherwise subject to Family Educational Rights and Privacy Act or Protection of Pupil Rights Amendment are described in Section 17.3 below.

10.2 Research Involving Pregnant Women, Human Fetuses and Neonates

The following applies to all research regardless of funding source. Since, according to the UIUC FWA, Subpart B of 45 CFR 46 applies only to DHHS-funded research, the funding source specific requirements are noted in the appropriate sections.

10.2.1 Definitions

Dead fetus - a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

Delivery - complete separation of the fetus from the woman by expulsion or extraction or any other means.

Fetus - the product of conception from implantation until delivery.

Neonate - a newborn.

Nonviable neonate - a neonate after delivery that, although living, is not viable.

Pregnancy encompasses the period of time from implantation until delivery. A woman is assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

Viable, as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.
10.2.2 Research Involving Pregnant Women or Fetuses

10.2.2.1 Research Not Funded by DHHS

For research where the risk to the fetus is no more than minimal and is not funded by DHHS, no additional safeguards are required and there are no restrictions on the involvement of pregnant women.

For research involving more than minimal risk to fetuses not funded by DHHS, pregnant women or fetuses may be involved 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 objectives 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 accord 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 accord 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;
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.
### 10.2.2.2 Research Funded by DHHS

For DHHS-funded research, 45 CFR Subpart B applies to all research involving pregnant women. Under 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 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 objectives 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 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 accord 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 accord 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 10.1.3;
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.

10.2.3 Research Involving Neonates
The following policies and procedures apply to all research involving neonates, regardless of funding source. Neonates of uncertain viability and nonviable 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 providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
3. Individuals engaged in the research will have no part in determining the viability of a neonate. 4. The requirements of Neonates of Uncertain Viability or Nonviable Neonates (see below in this section) have been met as applicable.

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:

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 accord 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.
Nonviable Neonates.

After delivery, nonviable 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 accord 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 nonviable 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 nonviable neonate will not suffice to meet the requirements of this paragraph.

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 accord with the requirements of IRB Review Process and Research Involving Children.

10.2.4 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 accord 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 manual are applicable.

10.2.5 Research Not Otherwise Approvable

10.2.5.1 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 (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB may approve the research based on either:

a. That the research in fact satisfies the conditions of Section 10.2.2, as applicable; or
b. The following:

1) 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;
2) The research will be conducted in accord with sound ethical principles; and
3) Informed consent will be obtained in accord with the provisions for informed consent and other applicable sections of this manual.

10.2.5.2 Research Funded by DHHS

DHHS-funded research that falls in this category must be approved by the Secretary of Health and Human Services. 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.

10.3 Research Involving Prisoners

Prisoners are another of the three classes that are 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. 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 concern that Subpart C, and this policy based
The following applies to all research involving prisoners, regardless of funding source. The requirements in this section are consistent with Subpart C of 45 CFR 46, which applies to DHHS-funded research.

10.3.1 Applicability
This policy applies to all research conducted under the auspices of UIUC involving prisoners as subjects. Even though a University IRB may approve a research protocol involving prisoners as subjects according to this policy, investigators are still subject to the Administrative Regulations of the Illinois Department of Corrections and any other applicable state or local law. [45 CFR 46.301]

10.3.2 Purpose
Because prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and non-coerced decision whether or not to participate as subjects in research, it is the purpose of this policy to provide additional safeguards for the protection of prisoners involved in research activities to which this subpart is applicable. [45 CFR 46.302]

10.3.3 Definitions
Prisoner – 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 which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

Minimal Risk – 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.

10.3.4 Composition of the IRB
In addition to satisfying the general requirements detailed in the IRB section of this manual, when reviewing research involving prisoners, the IRB must also meet the following requirements:
1. 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.

2. 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 satisfy this requirement.

10.3.5 Additional Duties of the IRB

In addition to all other responsibilities prescribed for IRB in the UIUC Institutional Review Board and IRB Review Process sections of this manual, the IRB will review research involving prisoners and approve such research only if it finds that:

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

2. any possible advantages accruing to the prisoner through his 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;

3. the risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;

4. 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 principal
investigator 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; 5. the information is presented in language which is understandable to the subject population; 6. 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 7. 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.

10.3.6 Waiver for Epidemiology Research
The Secretary of DHHS has waived the applicability of 45 CFR 46.305(a)(1) and 46.306(a)(2) for certain research conducted or supported by DHHS that involves epidemiologic studies that meet the following criteria:

1. In which the sole purposes are
   i. To describe the prevalence or incidence of a disease by identifying all cases, or
   ii. 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
   i. The research presents no more than minimal risk and no more than inconvenience to the prisoner-subjects, and ii. Prisoners are not a particular focus of the research.

The specific type of epidemiological research subject to the waiver involves no more than minimal risk and no more than inconvenience to the human subject participants. The waiver would allow the conduct of minimal risk research that does not now fall within the categories set out in 45 CFR 46.306(a)(2). 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 to the subjects. 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.

10.4 Persons with Mental Disabilities or Persons with Impaired Decision-Making Capacity
Research involving subjects who are mentally ill or subjects with impaired decision-making capacity warrants special attention. Research involving these populations may present greater than minimal risk; may not offer direct medical benefit to the subject; and may include a research design that calls for washout, placebo, or symptom provocation. In addition, these populations are considered to be vulnerable to coercion.

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.

10.4.1 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.

10.4.2 Approval Criteria
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 are suitable as research subjects. Competent persons are not suitable for the proposed research. The investigator 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 care agents [appointed under Durable Power of Attorney for Health Care (DPAHC)] or 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.

10.4.3 Additional Concerns
Both investigators 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 surrogate consent may be necessary. It is the responsibility of investigators to monitor the decision-making capacity of subjects enrolled in research studies and to determine if surrogate consent must be re-obtained.

The IRB will require investigators to conduct a competency assessment whenever there is a possibility of either impaired mental status or decision-making capacity in prospective subjects. The IRB will evaluate whether the proposed plan to assess capacity to consent is adequate. If feasible, the investigator must explain the proposed research to the prospective research subject even when the surrogate gives consent. Under no circumstances may a subject be forced or coerced to participate in a research study. The IRB will evaluate whether a) the assent of the subjects is required, and b) the plan for obtaining assent is adequate.

11 Complaints, Non-compliance, and Suspension or
Termination of IRB Approval of Research

11.1 Complaints
Complaints reported to the IRB will be evaluated as possible unanticipated events involving risks to participants or others under Section 7.8.

The Chair of the IRB and the Director of the OPRS 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.

11.2 Non-compliance
All members of the University community involved in human subject research are expected to comply with the highest standards of ethical and professional conduct in accordance with federal and state regulations and institutional and OPRS policies governing the conduct of research involving human subjects.

11.2.1 Definitions
“Non-compliance” is defined as 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 defined as failure to follow any of the regulations and policies described in this document or failure to follow the determinations of the IRB and which, in the judgment of either the IRB Chair or the convened IRB, increases risks to participants, decreases potential benefits, or compromises the integrity of the human research protection program. Research being conducted without prior IRB approval is considered serious noncompliance.

“Continuing non-compliance” is defined as a pattern of non-compliance that, in the judgment of the IRB Chair 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.

“Allegation of Non-Compliance” is defined as an unproved assertion of non-compliance.
“Finding of Non-Compliance” is defined as an allegation of non-compliance that is proven true or a report of non-compliance that is clearly true. (For example, 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.)

11.2.2 Review of Allegations of Non-compliance
All allegations of non-compliance will be reviewed by the IRB Chair and Director. They will review:

1. All documents relevant to the allegation;
2. The last approval letter from the IRB;
3. The last approved IRB application and protocol;
4. The last approved consent document.
5. The grant, if applicable; and
6. Any other pertinent information (e.g., questionnaires, DSMB reports, etc.).

The IRB Chair and Director will review the allegation and make a determination as to the truthfulness of the allegation. They may request additional information or an audit of the research in question. If in the judgment of the IRB Chair and Director, the reported allegation of non-compliance is not true, no further action will be taken. If in the judgment of the IRB Chair and/or Director, the reported allegation of non-compliance is true, the non-compliance will be processed according to 11.2.3 Review of Findings of Non-compliance.

If in the judgment of the IRB Chair and Director, any allegation or findings of noncompliance 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 may suspend the research as described below in Section 11.3 with subsequent review by the IRB.
11.2.3 Review of Findings of Non-Compliance
If in the judgment of the IRB Chair and Director, the reported finding of non-compliance is not serious, not continuing, and the proposed corrective action plan seems adequate, no further action is required and the IRB is informed at the next convened meeting. Otherwise, the matter will be presented to the IRB at a convened meeting with a recommendation that a formal inquiry (described below) will be held. All findings of non-compliance referred to the IRB will be reviewed at a convened meeting. All IRB members will receive:
1. All documents relevant to the allegation;
2. The last approval letter from the IRB;
3. The last approved IRB application; and
4. The last approved consent document.

At this stage, the IRB may:
1. Find that there is no issue of non-compliance;
2. Find that there is noncompliance that is neither serious nor continuing and an adequate corrective action plan is in place;
3. Find that there may be serious or continuing non-compliance and direct that a formal inquiry (described below) be held; or
4. Request additional information.

11.2.4 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 adverse events 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 full IRB at its next meeting;
6. Recommend actions if appropriate.

11.2.5 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. Modification of the protocol;
10. Modification of the information disclosed during the consent process;
11. Requiring current participants to re-consent to participation;
12. Suspend the study (See below); or
13. Terminate the study (See below).
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 11.4.

**11.2.6 Additional Actions**

A finding of serious or continuing non-compliance may also result in the following sanctions, among others:

1. **Suspension or termination of IRB approval of specific research protocols or of all research involving human subjects in which the investigator participates.**

2. **Sponsor actions.** In making decisions about supporting or approving applications or proposals covered by this policy the Department of Health and Human Services or Agency head may take into account, in addition to all other eligibility requirements and program criteria, factors such as whether the applicant has been subject to a termination or suspension as described above, and whether the applicant or the person or persons who would direct or have directed the scientific and technical aspects of an activity has/have, in the judgment of the Department of Health and Human Services or Agency head, materially failed to discharge responsibility for the protection of the rights and welfare of human subjects.

3. **Institutional or individual action by the federal OHRP.** The OHRP may
   - withhold approval of all new UIUC studies by the IRB;
   - direct that no new subjects be added to any ongoing studies;
   - terminate all ongoing studies, except when doing so would endanger the subjects; and/or
   - notify relevant state, federal and other interested parties of the violations.

4. **Individual disciplinary action** of the investigator or other personnel involved in a study, up to and including dismissal, pursuant to University policies and procedures.

Failure to secure necessary UIUC OPRS approval before commencing human subject research must be reported to the appropriate Dean and Vice Chancellor for Research for disciplinary action.
Investigators should also be aware that, in general, UIUC indemnifies them from liability for adverse events that may occur in UIUC studies approved by the UIUC IRB. Failure to follow approved procedures may compromise this indemnification and make the investigator personally liable in such cases.

11.3 Suspension or Termination
Suspension of IRB approval is a directive of the convened IRB or IRB Chair or OPRS Director to either to temporarily or to permanently stop some or all previously approved research activities short of permanently stopping all previously approved research activities. Suspended protocols remain open and require continuing review. Termination of IRB approval is a directive of the convened IRB to stop permanently all activities in a previously approved research protocol. Terminated protocols are considered closed and no longer require continuing review.

The IRB Chair or Director may suspend research to ensure protection of the rights and welfare of participants. Suspension directives made by the IRB Chair or OPRS Director must be reported to a meeting of the convened IRB.

Research may only terminated by the convened IRB. Terminations of protocols approved under expedited review must be made by the convened IRB. The IRB can suspend or terminate approval of research that is not being conducted in accordance with the IRB’s requirements or has been shown to have caused unexpected harm to participants.

When study approval is suspended or terminated by the convened IRB or an authorized individual, in addition to stopping all research activities, the convened IRB or individual ordering the suspension or termination will notify any subjects currently participating that the study has been suspended or terminated. The convened IRB or individual ordering the suspension or termination will consider whether procedures for withdrawal of enrolled subjects are necessary to protect their rights and welfare of subjects, such as: transferring participants to another investigator; making arrangements for care or follow-up outside the research; allowing continuation of some research activities under the supervision of an independent monitor; or requiring or permitting follow-up of participants for safety reasons.
If follow-up of subjects for safety reasons is permitted/required by the convened IRB or individual ordering the suspension or termination, the convened IRB or individual ordering the suspension or termination will require that the subjects should be so informed and that any adverse events/outcomes be reported to the IRB and the sponsor.

11.4 Reporting
Serious or continuing noncompliance with regulations or the requirements or determinations of the IRB; and suspensions or terminations of IRB approval will be reported to the appropriate regulatory agencies and institutional officials according to the procedures in Section 12.

12 Reporting to Regulatory Agencies and Institutional Officials
The OPRS office will initiate the following procedures as soon as the IRB takes any of the following actions:

a) Determines that an event may be considered an unanticipated problem involving risks to participants or others;

b) Determines that non-compliance was serious or continuing;

c) Suspends or terminates approval of research.

12.1 Procedures
1. The OPRS Director or designee prepares a letter that contains the following information:

a) The nature of the event (Unanticipated problem involving risks to participants 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
   (1) A specific date; or
   (2) When an investigation has been completed or a corrective action plan has been implemented.

2. The IRB Chair and the Institutional Official review the letter and modify the letter as needed.

3. The Institutional Official signs the letter and returns it to the Director or designee.

4. 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 Institutional Official;
   c) OHRP, if the study is subject to DHHS regulations or subject to a DHHS federalwide assurance;
   d) The FDA when the research involves drugs or devices which are regulated by the FDA;
   e) 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;
      • 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;
   f) Principal investigator;
   g) The Department of Defense when research is sponsored by DoD;
   h) Other sponsors, if the study is sponsored;
   i) Contract research organization, if the study is overseen by a contract research organization;
   j) Chairman or supervisor of the principal investigator;
   k) The Privacy Officer of a covered entity, if the event involved unauthorized use, loss, or disclosure of individually-identifiable patient information from that covered entity;
I) The Information Security Officer of an organization if the event involved violations of information security requirements of that organization;

m) Others as deemed appropriate by the Institutional Official.

The Director ensures that all steps of this policy are completed within 15 days of the initiating action. For more serious actions, the Director will expedite reporting.

13 Investigator Responsibilities

Responsible Principal Investigators are ultimately responsible for the conduct of research. Principal Investigators may delegate research responsibility. However, investigators must maintain oversight and retain ultimate responsibility for the conduct of those to whom they delegate responsibility. In order to satisfy the requirements of this policy, investigators who conduct research involving human subjects must:

• develop and conduct research that is in accordance with the ethical principles in the Belmont Report
• develop a research plan that is scientifically sound and minimizes risk to the subjects;
• have sufficient resources necessary to protect human subjects, including:
  o access to a population that would allow recruitment of the required number of subjects
  o sufficient time to conduct and complete the research
  o adequate numbers of qualified staff
  o adequate facilities
  o a process to ensure that all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions.
  o availability of medical or psychological resources that subjects might require as a consequence of the research
• protect the rights and welfare of prospective subjects;
• have plans to monitor the data collected for the safety of research subjects,
• have a procedure to receive complaints or requests for additional information from subjects and respond appropriately,
• ensure that pertinent laws, regulations, and institution procedures and guidelines are observed by participating faculty and research staff;
• 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;
• ensure that all research involving human subjects receives IRB review and approval in writing before commencement of the research;
• comply with all IRB decisions, conditions, and requirements;
• ensure that protocols receive timely continuing IRB review and approval;
• report unexpected or serious adverse events problems that require prompt reporting to the IRB (see Section 7.8.1.1)
• obtain IRB review and approval in writing before changes are made to approved protocols or consent forms
• seeking IRB assistance when in doubt about whether proposed research requires IRB review
• use the most current form available on the IRB website

13.1 Investigators
Responsible Principal Investigators
At UIUC only non-visiting faculty or staff members with University-paid appointments may serve as the Responsible Principal Investigator or as the faculty sponsor on a research project involving human subjects. Adjunct or visiting faculty of the University may not serve as a Principal Investigator but may serve as a co-investigator.

The OPRS recognizes one Responsible Principal Investigator (RPI) for each study. The RPI has ultimate responsibility for the research activities.

Protocols that require skills beyond those held by the Responsible Principal Investigator must be modified to meet the investigator's skills and/or have one or more additional qualified faculty as Coinvestigator(s).

Student Investigators
Students, both undergraduate and graduate, may not serve as Responsible Principal Investigators. They must have a faculty sponsor who fulfills the RPI eligibility criteria and who will serve as Principal Investigator and faculty advisor on the study.
Research Team
The research team includes the RPI 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.

13.2 Protocol Development
When developing a protocol, the Responsible Principal Investigator or a member of the protocol research team may contact the OPRS Office for a determination whether the proposed project constitutes human subjects research, and if so, what level of review would be required. Contact with the OPRS Office may be in the form of a phone call, letter, or email and must include a brief description of the proposed research. The OPRS Office will respond to the RPI or member of the research team by phone, letter, or email.

Investigators must provide complete answers to all questions on the Initial Application Form (IRB-1) and make certain that consent information is in agreement with the research plan.

Proposed consent/assent form (if applicable) must include or address:

1. The General Principles and Basic Elements of Informed Consent
2. Translated consent documents, as necessary, considering likely subject population(s)
3. UIUC IRB-approved formats for consent forms and assent forms or
4. a request for a waiver of informed consent.

If necessary, the investigator must submit the IRB protocol submission form and all attachments to appropriate institutional regulatory committee offices (e.g., Radiation Safety Committee, Institutional Biosafety Committee, etc.) for review and sign-off.

If research is DHHS-sponsored, materials delivered to the IRB reviewer must include the entire sponsoring application; if there is a significant variation between the DHHS application and the IRB protocol, the investigator must identify and justify the discordance.
If research is FDA-regulated and industry-sponsored, materials delivered to the IRB must include the entire sponsor's protocol as well as, for drug studies, the investigator's brochure [21 CFR 312.23(a)(5) and 312.55], FDA form 1572, and the sponsor Financial Disclosure form.

Following departmental review and sign-off by Department Chairs (when appropriate) or other appropriate institutional official, the investigator must submit an electronic copy to the UIUC OPRS Office.

Investigators should contact the OPRS Office before submission of documents to determine the number of copies to be submitted.

Note: Investigators who have other individuals write their protocols and draft responses to the IRB must recognize that the ultimate responsibility of any study lies with the Responsible Principal Investigator (RPI). It is incumbent upon the RPI to check all material that is submitted to the OPRS for review.

13.3 Changes to Approved Research
Investigators must seek IRB approval before making any changes in approved research even though the changes are planned for the period for which IRB approval has already been given unless the change is necessary to eliminate an immediate hazard to the subject (in which case the IRB must then be notified at once). Minor changes (i.e., changes that do not involve increased risk or discomfort) may be authorized by the IRB Chair or his/her designee. A letter specifying the changes requested, a revised consent form (if applicable), and a copy of the approved protocol with the proposed changes highlighted, should be sent directly to IRB Office. The IRB Chair or Director of the IRB Office must sign and return a letter to indicate approval.

Note: IRB approved amendments to ongoing research do NOT extend the original approval expiration date.

13.4 Continuing Review after Protocol Approval
Ongoing research studies must be reviewed by the IRB at least annually, or more often, if the IRB finds that the degree of risk to subjects warrants more frequent review. This renewal must take place prior to the end of the approval period noted on the approved protocol; otherwise, subject
recruitment/enrollment must be suspended and, if the research is DHHS-sponsored, the Agency must be notified.

It is the responsibility of the RPI to submit a timely continuing review application. As a courtesy, the UIUC IRB Office will send a “Request for Continuation” form to the RPI two months prior to the expiration of each approved protocol. The investigator should allow sufficient time for development and review of renewal submissions.

**Note:** The "approval date" and the "approval expiration date" are listed on all IRB certifications. Investigators must provide complete answers to all questions on the Protocol Renewal Form.

### 13.5 Required Reports to the IRB

#### 13.5.1 Unanticipated Problems

Principal investigators must report to the OPRS as soon as possible, but in all cases within 5 working days, of any:

1. Adverse events which in the opinion of the principal investigator are both unexpected and related to the research;
2. 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;
3. 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.
4. A breach of confidentiality;
5. Incarceration of a participant in a protocol not approved to enroll prisoners;
6. Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant;
7. Complaint of a participant when the complaint indicates unexpected risks or cannot be resolved by the research team;

8. 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;

9. Event that requires prompt reporting to the sponsor;

10. Sponsor imposed suspension for risk.

13.5.2 Complaints, Non-compliance and Protocol Deviations
Investigators must report all complaints and concerns from subjects, non-compliance by research staff, and any protocol deviations to the OPRS within ten (10) working days as described in Section 7.8.1.1 for evaluation as possible unanticipated problems involving risks to subjects or others.

13.5.3 Progress Reports
Investigators must report the progress of the research to the OPRS in the manner and frequency prescribed by the IRB, but no less than once a year.

Once data collection has been completed and the research is closed at either the University or other sites, the Principal Investigator is not required to submit any further reports of the research to the IRB.

13.6 Investigator-Required Record Keeping
Investigators must retain copies of approved IRB documents, and implement a system to ensure compliance with approval expiration dates.

In addition to providing a copy of the signed and dated consent form to each subject, a copy must be stored securely by the Principal Investigator (RPI) and placed in the subject's file or medical record (if the subject is a patient and this requirement has not been waived by the IRB), and a copy must be retained by the RPI for a minimum of 3 years after completion of the research.

13.7 Investigators or Research Personnel Conflicts of Interest
All Investigators and key research personnel must follow the University of Illinois Policy on Conflicts of Commitment and Interest (COCI Policy).
As part of its general financial disclosure, the University will ask if any related research involves human subjects. If yes, the investigator will work with the unit head and the Associate Vice Chancellor for Research who is an ex officio member of the Conflict of Interest Committee to develop a conflict management plan. A copy of the final, approved conflict management plan will be filed with OPRS.

The IRB application asks protocol-specific questions regarding conflict of interest for the investigators and key personnel. As part of its review process, the IRB will make a determination as to whether the conflict adversely affects the protection of human subjects. If a conflict of interest exists, final IRB approval cannot be given until an approved conflict management plan that adequately protects the human subjects in the protocol is in place.

If the conflict of interest status of an investigator changes during the course of a study, the individual is required to notify the OPRS within ten (10) working days of the change. The IRB will review the change as a modification to the protocol.

At the time of continuing review, the investigator will be asked whether there has been any change in the conflict of interest status relating to the research. The OPRS will review conflict of interest as part of its continuing review.

### 13.8 Training / Ongoing Education of Principal Investigator and Research Team

One component of a comprehensive human research protection program is an education program for all individuals involved with research subjects. UIUC is committed to providing training and an on-going educational process for investigators and members of their research team related to ethical concerns and regulatory and institutional requirements for the protection of human subjects.

**Orientation**

All Responsible Principal Investigators and members of their research team (also known as “key personnel”) must review core training documentation including:

- the “Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research” and,
- the UIUC Investigator’s Handbook.

All of these can be found on the OPRS website.

**Initial Education**
The RPI and all key personnel must complete one of the following core basic trainings in the Protection of Human Research Subjects on the CITI Program:

1. Required UIUC Training Modules;
2. Social and Behavioral Research;
3. Biomedical Research.

Initial education certification is good for three (3) years, after which recertification and continuing education requirements must be met.

New research protocols and applications for continuing review will not be accepted from principal investigators who have not completed the initial education requirement (or the continuing education requirement once the initial education requirement has been satisfied).

While research protocols and applications for continuing review will be accepted and reviewed if the RPI holds a current certification of training, final approval will not be granted until all co-investigators and members of the research team have completed the initial education requirement (or the continuing education requirement once the initial education requirement has been satisfied).

**Waiver of Initial Education**
If investigators or members of their research team can verify that they have successfully completed human subjects research training equivalent to that required by the University, they may request a waiver of the requirement for Initial Education. However, these investigators or members of their research team must complete the requirements for Continuing Education.
Continuing Education and Recertification

All investigators and members of their research teams must meet UIUC 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. Review of appropriate modules at the CITI Program web-based training site is required.

Additional Resources

Human research protection information will be made available on the OPRS website on an ongoing basis to ensure that the University research community is apprised of current regulatory and policy requirements and training opportunities.

13.9 Subject Recruitment

Investigators are responsible for recruiting research subjects in a manner that is fair, ethical and equitable. IRB approval is required for all recruitments procedures and materials. Recruitment materials must be consistent with the approved IRB protocol, accurate, and not coercive. Recruitment materials should adequately describe the remuneration associated with services as a research subject, but shall not be displayed in such a manner as to emphasize payment as the primary incentive for involvement in the research.

13.10 Payment to Subjects

Payment to research subjects may be an incentive for participation or a way to reimburse a subject for travel 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.

The IRB must review both the amount of payment and the proposed method of disbursement to assure that neither entails problems of coercion or undue influence.
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 IRB does not allow the entire payment to be contingent upon completion of the entire study. Payment in exchange for referrals of prospective participants from researchers/physicians (“finder’s fees”) is not permitted. Similarly, payment designed to accelerate recruitment that is tied to the rate or timing of enrollment (“bonus payments”) is also not permitted.

The consent form 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 UIUC Office of Business and Financial Services requires identifying information to issue checks, cash, or gift certificates to subjects. The consent form must 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. For confidential studies, only name and address are required by OBFS, but the RPI MUST keep an identity key in a secure place.

13.11 Investigator Concerns
Investigators who have concerns or suggestions regarding UIUC’s human research protection program should convey them to the Institutional Official (Vice Chancellor for Research) or other responsible parties (e.g. college dean, departmental Chair, etc.) regarding the issue, when appropriate. The Institutional Official 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 Chair of the IRB or the Director of the OPRS will be available to address investigators’ questions, concerns and suggestions.

14 Health Insurance Portability and Accountability Act
The Health Insurance Portability and Accountability Act of 1996 (HIPAA) required the creation of a Privacy Rule for identifiable health information. The resulting Privacy Rule, finalized in August 2002, set a compliance date of April 14, 2003. While the main impact of the Privacy Rule will be on the routine provision of and billing for health care, the Rule will also affect the conduct and oversight of research. Researchers, OPRS staff and IRB members as well as research administration must be aware of these changes.

14.1 Historical Background
The Health Insurance Portability and Accountability Act of 1996 (HIPAA) is an expansive federal law, only part of which is intended to protect the privacy of health care information. HIPAA required Congress to enact a health information privacy law by August 1999 and stated that if it did not act by then, which it did not, the U. S. Department of Health and Human Services (DHHS) must develop privacy regulations. The final Privacy Rule was published on August 14, 2002.

The objective of the rule is to protect the privacy of an individual's health care information. It creates a federal "floor" of protection so that every person in this country has at least the same basic rights and protections, though some may have additional rights depending on state law.

14.2 Effects of HIPAA on Research
The final Privacy Rule published on August 14, 2002 included a number of changes in how the Rule applies to research. See the NIH HIPAA Privacy Rule Booklet for Research and the NIH fact sheet on Institutional Review Boards and HIPAA for more information on how HIPAA applies to research. See also Impact of the Privacy Rule on Academic Research, a white paper published by the American Council on Education.

University of Illinois at Urbana Champaign is not a covered entity under HIPAA. However, researchers who are working with “Protected Health Information” (PHI) from other institutions that are covered entities will need to comply with the rules on HIPAA.
14.3 Research under HIPAA
HIPAA defines research as "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge."

This definition is identical with the one used in the so-called “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’ (not animals’) health information.

14.4 HIPAA and New Documentation Requirements
New research documents include a HIPAA authorization form, a waiver of authorization form, and a deidentification form. These documents must be used whenever PHI of a covered entity is being utilized in the research.

14.5 Patient Rights and Research
Under HIPAA, patients have certain new 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.

14.6 HIPAA and Existing Studies
Any research subject enrolled in a study that uses PHI from a covered entity must sign a HIPAA-compliant authorization form. This form is in addition to the existing Informed Consent document, and is federally required. In a few cases, the Informed Consent document may be combined with a HIPAA authorization.

14.7 Waivers to HIPAA Forms
In some cases an IRB may approve a waiver to use of the HIPAA authorization form. This may occur when the IRB finds that the research could not be practically done without the waiver, and not without access to and use of the PHI, and that disclosure poses minimal risk to privacy. This waiver would generally come from the IRB of the covered entity that has “ownership” of the PHI. When a covered entity enters into an Institutional Authorization Agreement to rely on the UIUC IRB it may choose to have the UIUC IRB approve the HIPAA waiver. The RPI should submit the waiver request with the IRB
application materials. Although the UIUC IRB does not review or approve HIPAA Authorization forms, these forms should be submitted with the IRB application materials to be retained with the protocol file.

15 Special Topics

15.1 Certificate of Confidentiality

15.1.1 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."

Certificates of Confidentiality constitute an important tool to protect the privacy of research study subjects. Certificates are issued by the National Institutes of Health (NIH) 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 subjects in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level.

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. For more information, see the NIH Certificates of Confidentiality Kiosk.

Certificates of Confidentiality will be issued automatically for applicable NIH awards as part of the award terms and conditions. The award itself may be used as confirmation that the Certificate of Confidentiality protections are in place. The NIH will not provide a paper certificate. The certificate goes beyond the consent form 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).

NIH considers research in which identifiable, sensitive information is collected or used, to include:

- Human subjects research as defined in the Federal Policy for the Protection of Human Subjects (45 CFR 46), including exempt research except for human subjects research that is determined to be exempt from all or some of the requirements of 45 CFR 46 if the information obtained is recorded in such a manner that human subjects cannot be identified or the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
- Research involving the collection or use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual;
- Research that involves the generation of individual level, human genomic data from biospecimens, or the use of such data, regardless of whether the data is recorded in such a manner that human subjects can be identified or the identity of the human subjects can readily be ascertained as defined in the Federal Policy for the Protection of Human Subjects (45 CFR 46); or
- Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some
combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual, as defined in subsection 301(d) of the Public Health Service Act.

15.1.2 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 informed consent form 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:

- the subject (or, if he/she is legally incompetent, his/her legal guardian) consents, in writing, to the disclosure of such information;
- authorized personnel of the Department of Health and Human Services (DHHS) request such information for audit or program evaluation, or for investigation of DHHS grantees or contractors and their employees; or
- release of such information is required by the Federal Food, Drug, and Cosmetic Act or regulations implementing that Act.

15.2 Mandatory Reporting
While any person may make a report if they have reasonable cause to believe that a child or elder was abused or neglected, Illinois law mandates that certain persons who suspect child or elder abuse or neglect report this to the Illinois Department of Children and Family Services (DCFS) or the Illinois Department on Aging, as appropriate. Effective in 2012, the Illinois Abused and Neglected Child Reporting Act (ANCRA) requires all personnel of higher education institutions to acknowledge their
understanding of their mandated reporting requirements should they witness or suspect abuse neglect of a minor. As such, ANCRA designates ALL UIUC personnel as mandated reporters.

UIUC policy requires the solicitation of informed consent from all adult research subjects and assent from children involved as research subjects, in addition to the consent of their parents. In situations where conditions of abuse or neglect might be revealed, mandated reporters should make themselves known as such to parents of children under age 18, to subjects who are children, and to subjects who are potential victims of elder abuse or neglect.

The Abused and Neglected Child Reporting Act (P.A. 79-65, cite 325 ILCS 5/1 et seq.), revised June, 2012 states (emphasis added):

"Sec. 4. Persons required to report; privileged communications; transmitting false report. Any physician, resident, intern, hospital, hospital administrator and personnel engaged in examination, care and treatment of persons, surgeon, dentist, dentist hygienist, osteopath, chiropractor, podiatric physician, physician assistant, substance abuse treatment personnel, funeral home director or employee, coroner, medical examiner, emergency medical technician, acupuncturist, crisis line or hotline personnel, school personnel (including administrators and both certified and non-certified school employees), personnel of institutions of higher education, educational advocate assigned to a child pursuant to the School Code, member of a school board or the Chicago Board of Education or the governing body of a private school (but only to the extent required in accordance with other provisions of this Section expressly concerning the duty of school board members to report suspected child abuse), truant officers, social worker, social services administrator, domestic violence program personnel, registered nurse, licensed practical nurse, genetic counselor, respiratory care practitioner, advanced practice nurse, home health aide, director or staff assistant of a nursery school or a child day care center, recreational or athletic program or facility personnel, early intervention provider as defined in the Early Intervention Services System Act, law enforcement officer, licensed professional counselor, licensed clinical professional counselor, registered psychologist and assistants working under the direct supervision of a psychologist, psychiatrist, or field personnel
of the Department of Healthcare and Family Services, Juvenile Justice, Public Health, Human Services (acting as successor to the Department of Mental Health and Developmental Disabilities, Rehabilitation Services, or Public Aid), Corrections, Human Rights, or Children and Family Services, supervisor and administrator of general assistance under the Illinois Public Aid Code, probation officer, animal control officer or Illinois Department of Agriculture Bureau of Animal Health and Welfare field investigator, or any other foster parent, homemaker or child care worker having reasonable cause to believe a child known to them in their professional or official capacity may be an abused child or a neglected child shall immediately report or cause a report to be made to the Department."

DCFS requires the following on its "Acknowledgment of Mandated Reporter Status" form (emphasis added):

"...I am required to report or cause a report to be made to the child abuse Hotline number (1800-25A-BUSE) whenever I have reasonable cause to believe that a child known to me in my professional or official capacity may be abused or neglected. . .I also understand that if I am subject to licensing under the Illinois Nursing Act of 1987, the Medical Practice Act of 1987, the Illinois Dental Practice Act, the School Code, the Acupuncture Practice Act, the Illinois Optometric Practice Act of 1987, the Illinois Physical Therapy Act, the Physician Assistants Practice Act of 1987, the Podiatric Medical Practice Act of 1987, the Clinical Psychologist Licensing Act, the Clinical Social Work and Social Work Practice Act, the Illinois Athletic Trainers Practice Act, the Dietetic and Nutrition Services Practice Act, the Marriage and Family Therapy Act, the Naprapathic Practice Act, the Respiratory Care Practice Act, the Professional Counselor and Clinical Professional Counselor Licensing Act, the Illinois Speech-Language Pathology and Audiology Practice Act, I may be subject to license suspension or revocation if I willfully fail to report suspected child abuse or neglect."

The Elder Abuse and Neglect Act (P.A. 85-1184, cite 320 ILCS 20/) effective January 1, 1999, states:

""Mandated reporter" means any of the following persons while engaged in carrying out their professional duties: (1) a professional or professional's delegate while engaged in: (i) social services, (ii) law enforcement, (iii) education, (iv) the care of an eligible adult or eligible adults,
or (v) any of the occupations required to be licensed under the Clinical Psychologist Licensing Act, the Clinical Social Work and Social Work Practice Act, the Illinois Dental Practice Act, the Dietetic and Nutrition Services Practice Act, the Marriage and Family Therapy Licensing Act, the Medical Practice Act of 1987, the Naprapathic Practice Act, the Nursing and Advanced Practice Nursing Act, the Nursing Home Administrators Licensing and Disciplinary Act, the Illinois Occupational Therapy Practice Act, the Illinois Optometric Practice Act of 1987, the Pharmacy Practice Act of 1987, the Illinois Physical Therapy Act, the Physician Assistant Practice Act of 1987, the Podiatric Medical Practice Act of 1987, the Respiratory Care Practice Act, the Professional Counselor and Clinical Professional Counselor Licensing Act, the Illinois Speech Language Pathology and Audiology Practice Act, the Veterinary Medicine and Surgery Practice Act of 1994, and the Illinois Public Accounting Act, (2) an employee of a vocational rehabilitation facility prescribed or supervised by the Department of Human Services; (3) an administrator, employee, or person providing services in or through an unlicensed community based facility; (4) a Christian Science Practitioner; (5) field personnel of the Department of Public Aid, Department of Public Health, and Department of Human Services, and any county or municipal health department; (6) personnel of the Department of Human Services, the Guardianship and Advocacy Commission, the State Fire Marshal, local fire departments, the Department on Aging and its subsidiary Area Agencies on Aging and provider agencies, and the Office of State Long Term Care Ombudsman; (7) any employee of the State of Illinois not otherwise specified herein who is involved in providing services to eligible adults, including professionals providing medical or rehabilitation services and all other persons having direct contact with eligible adults; or (9) a person who performs the duties of a coroner or medical examiner."

Investigators should consult these sources to determine if potential subjects should be advised of mandatory reporting requirements during the informed consent process.

15.3 UIUC Students and Employees as Subjects
When UIUC 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 their grades at, status at, or future relations with the University of Illinois will NOT be affected by their participation decision.

To minimize coercion, investigators should avoid, whenever possible, the use of their own students and employees in research 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 other than their own. When entering a classroom to recruit students and/or conduct research, 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.

15.4 Departmental Subject Pool

Department of Psychology

The Department of Psychology subject pool consists of all students enrolled in Psychology 100. Each Psychology 100 student must complete six hours of research for course credit. Students who do not wish to participate in research projects will be provided with an alternate equivalent task in order to earn the required credit.

The Department of Psychology conducts all research and training in accordance with the ethical guidelines set forth by the American Psychological Association, and as appropriate, with the approval of UIUC’s Institutional Review Board.

Department of Educational Psychology

The Department of Educational Psychology has a Subject Pool that may be utilized to serve as a source of subjects for researchers in all six departments in the College of Education and occasionally for researchers from other departments outside the College. OSURR manages the Subject Pool on behalf of the Educational Psychology Department.
Students who enroll in one of the following Educational Psychology courses (201, 220, 236, 400, 404, and 485) are notified at the time of enrollment that as part of the course requirements they are expected to serve as research subjects in the subject pool for a designated number of hours.

15.5 Student Research

15.5.1 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.)
- 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 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 about the ethical conduct of research and about the preparation of the IRB application 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 OPRS Office for assistance (irb@illinois.edu or 217-333-2670). UIUC policy and procedures, educational modules, forms and other related information can be found on the UIUC IRB website at: www.irb.illinois.edu.

Individual Research Projects Conducted by Students
Independent study projects, senior theses, undergraduate research projects, master’s and advanced degree research, and similar exercises 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 subjects and collecting data. IRB review cannot occur after a study has begun. Students and advisers should contact the OPRS Office (irb@illinois.edu or 217-333-2670) with any questions.

15.5.2 Independent Study, Theses and Dissertations
These research activities are considered to meet the definition of human subjects research and must be submitted to the IRB by the student-researcher. However, when students conduct research as part of a course of study, a faculty member ultimately is responsible for the protection of the subjects and serves as the RPI, even if the student is the primary researcher and actually directs the project. Advisers assume the responsibility for students engaged in independent research, and instructors are responsible for research that is conducted as part of a course.
Note: Students may not serve as Responsible Principal Investigators. They must have a faculty sponsor who fulfills the principal investigator eligibility criteria and who will serve as Principal Investigator and faculty adviser on the study.

15.6 Oral History
The following is based on guidance received from OHRP:

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 research subjects (45 CFR 46) 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."

Specifically, for the purposes of this policy, the evaluation of such activities hinges upon whether:

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.

In order to be subject to the University’s human research protections policies, the activity must meet both of the above standards. This determination will be made according to the procedures described in Section 7.1 Human Subjects Research Determination.

General principles for evaluating Oral History type activities:
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" as defined by HHS regulations 45 CFR part 46.

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" as defined by HHS regulations at 45 CFR 46.

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 would require IRB review and approval.

3. 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 as defined by 45 CFR 46, the creation of such an archive WOULD constitute research under 45 CFR 46.

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 under 45 CFR part 46 since the intent is to collect data for future research.

Investigators are advised to consult with the OPRS Office regarding whether their oral history project requires IRB review.

15.7 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.

In studies involving genetic testing, several questions need to be addressed, including:

1. Will test results be given?
2. Will disease risk be quantified, including the limits on certainty of the testing?
3. Will a change in a family relationship be disclosed, such as mistaken paternity?
4. Does the subject or family member have the option not to know the results? How will this decision be recorded?
5. Could other clinically relevant information be uncovered by the study? How will disclosure of this added information occur?
6. Do any practical limitations exist on the subject's right to withdraw from the research, withdraw data, and/or withdraw DNA?
7. 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)?

For DNA banking studies, several questions need to be addressed, including:

1. Will DNA be stored or shared? If shared, will the subject's identity be known by the new recipient investigator?
2. Will the subject be contacted in the future by the investigator to obtain updated clinical information?
3. How can the subject opt out of any distribution or subsequent use of his/her genetic material?

15.8 Research Involving Coded Private Information or Biological Specimens
UIUC policy in this area is based on the OHRP guidance document entitled, “Guidance on Research Involving Coded Private Information or Biological Specimens” (August 10, 2004). 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 research subjects (45 CFR 46).
• Reaffirms OHRP policy that, under certain limited conditions, research involving only coded private information or specimens is not human subjects research.
• Provides guidance on who should determine whether human subjects are involved in research.

For purposes of this policy, **coded** means that: (1) identifying information (such as 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 pertain 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 identifying information to the private information or specimens.

Under the definition of **human subject** in Section 2 of this policy, obtaining identifiable private information or identifiable specimens for research purposes constitutes human subjects research. **Obtaining** means receiving or accessing identifiable information or identifiable specimens for research purposes. This includes an investigator’s use, study, or analysis for research purposes of identifiable private information or identifiable specimens already in the possession of the investigator.

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 pertain because, for example:
   (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); 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 individuals are 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 (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 pertain, then the research activity now would involve human subjects. Unless this human subjects research is determined to be exempt (See Section 7.2), 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 9.3).

**Who Should Determine Whether Coded Private Information or Specimens Constitutes Human Subjects Research**

The investigator in consultation with the IRB Chair or Director of the IRB Office 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 email, it is the investigator’s responsibility to maintain documentation of such a decision. If the investigator 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/email will be kept on file.
15.9 Transnational Research

When conducting research outside of the United States, protocols are to meet certain criteria before study-related research may commence. Procedures normally followed outside the United States for research engaging human subjects may differ from those mandated in federal and institutional policies. These may be the result from differences in language, culture, social history, and societal norms.

Researchers are to be cognizant of relevant national policies and take special consideration in cases such as, the availability of national health insurance, different philosophical legal systems, and social policies that may make U.S. research forms and procedures inappropriate. Investigators will ensure full disclosure of the nature of their research to participants and follow an informed consent process appropriate to the population. Requests for waivers of informed consent and waivers of documentation of informed consent in these cases will be considered carefully by the IRB.

Approval will be sought from local IRBs or Independent Ethic Committees. Documentation of permission or approval must be submitted with the IRB application materials. In the absence of these laws or guidance, the researcher is required to obtain approval from the local government or community leaders or provide information as to the absence of the local review. Examples of local reviews may include the following:

- Ethics committees
- Drug approval agencies
- Local ministries
- Local governance

At the time of initial review, the investigator must demonstrate that he/she and key project personnel possess the appropriate qualifications for conducting research in a specific country or region. The Data Collected in Transnational Sites document is used to provide information to evaluate the qualifications of the research personnel.
For initial and continuing review if there is no IRB member familiar with local context the IRB will consult with University faculty, transnational campus organizations or community individuals experienced in the local law, culture and social values of the community where the research will take place.

**15.10 Outreach to Research Participants**
The university and the OPRS have the responsibility to inform research participants about their rights as research participants and to create a safe atmosphere in which current or prospective research participants may voice questions, comments or concerns about research participation, obtain information about research, or provide feedback about university sponsored research.

The university provides informational materials in print, on the IRB website or through other media to meet this responsibility. Research participants are directed to contact the OPRS to ask questions, voice concerns or complaints or obtain information in a confidential manner at no expense.

Outreach activities are evaluated annually by the Vice Chancellor for Research (or designee), the IRB chair, by other interested members of the IRB and other university and community stakeholders as appropriate. In addition, it will be informally reviewed on an as needed basis, by the OPRS staff. Concerns, complaints, input, or suggestions regarding the Human Research Protection Program and all allegations of coercion, undue influence, or noncompliance are thoroughly investigated and, if applicable, corrective actions will be taken. The HRPP Director is responsible for assuring that all issues have been addressed appropriately and may delegate administrative staff to follow-up with researchers and subjects, if necessary. If the concern/complaint could entail researcher noncompliance, further inquiry will follow procedures outlined in Section 11.2. If the concern/complaint appears to involve an unanticipated problem involving risks to subjects or others, it will be reviewed according to Section 7.8 of this policy and procedure manual.

**16 FDA Regulated Research – Research Involving the Use of Drugs, Biologics or Medical Devices**
Under FDA regulations, an activity is considered to be human subject research when any of the following are true:
1. The activity is conducted in the United States and involves the use of a drug in one or more persons that is NOT the use of an approved drug in the course of medical practice.

2. The activity evaluates the safety or effectiveness of a device in one or more persons.

3. Data regarding subjects be submitted to or held for inspection by the FDA as part of an application for a research or marketing permit.

4. Data regarding the use of a device on human specimens be submitted to or held for inspection by the FDA as part of an application for a research or marketing permit.

16.1 Definitions

**Clinical Investigation:** Any experiment in which a test article is administered or dispensed to, or used involving, one or more human subjects. In this context, experiment refers to any use of a drug except for the use of a marketed drug in the course of medical practice. (21 CFR 312.3(b))

**Drug:** A product that is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease or intended to affect the structure or function of the body and achieves its intended effect through chemical action or metabolism within or on the body.

**Emergency Use:** The use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

**Food and Dietary Supplements** generally are not regulated as drugs. However, those that are intended or promoted to be used in the diagnosis, cure, mitigation, treatment or prevention of disease are considered drugs.

**Biologic:** A biological or related product derived from living sources (e.g., humans, animals, microorganisms) and regulated by the FDA, including blood, vaccines, allergenics, tissues and cellular and gene therapies. Studies of unlicensed biologics are generally regulated according to the IND regulations. FDA regulations related to the general use and licensing of biologics are found in 21 CFR 600 and 601.
Investigational New Drug Application (IND): An IND exempts an investigational new drug from premarketing approval requirements that would otherwise be applicable and allows the drug to be lawfully shipped for the purpose of conducting clinical investigations of that drug (21 CFR 312.1(a)).

Investigational New Drug: An unapproved drug or biologic (or approved drug or biologic for an unapproved indication) used in an FDA-regulated clinical investigation. The term also includes biological products used in vitro for diagnostic purposes. Clinical investigations that involve FDA regulated drugs are subject to the requirements of 21 CFR 312.

Device: An instrument, apparatus, machine or similar article that is used for the diagnosis, mitigation, cure, prevention or treatment of disease and does not work through chemical action or metabolism within the body.

Investigational Device Exemption Application (IDE): An IDE exempts an unapproved or uncleared device (or an approved or cleared device for an unapproved or uncleared indication) in a research study involving humans (i.e., an IDE is an investigational exemption) from certain statutes and regulations. With this exemption, the unapproved or uncleared device can be shipped and used in human research.

Investigational Device: A medical device that is the subject of a clinical study designed to evaluate the effectiveness or safety of the device, or a clinical evaluation of certain modifications or new intended uses of a legally marketed device. Clinical investigations that involve FDA regulated devices are subject to the requirements of 21 CFR 812.

Premarket Approval (PMA) Application: A PMA is the most stringent type of marketing application for medical devices; FDA approves a PMA based on presence of sufficient valid scientific evidence and reasonable assurance that the device is safe and effective for its intended use. Once approved, it can be marketed and sold within its approved labeling.
Premarket Notification (510(K)): A 510(k) application is submitted to FDA before a manufacturer plan to market a device. If the FDA agrees that the new device is substantially equivalent to a legally marketed device for which a PMA is not required, the manufacturer may market it immediately. FDA does not require clinical data for most 510(k)s. However, if clinical data are necessary to demonstrate equivalence, the clinical study must comply with IDE, IRB and human subject protection regulations.

Significant Risk Device: Significant risk device (SR) is an investigational device that: (1) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; (2) is for use in supporting or sustaining human life and represents a potential for serious risk to the health, safety, or welfare of a subject; (3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or (4) otherwise presents a potential for serious risk to a subject. The SR determination encompasses the proposed use and not the device alone (e.g., need for additional procedures, such as surgical implantation, as part of the study should be included in risk assessment.

Nonsignificant Risk Device: A device not meeting the definition of SR device. Examples of significant and nonsignificant risk devices are available at:

Test article: any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation.

16.2 Policy
The UIUC IRB follows federal, state and institutional regulations in reviewing research involving the use of drugs, biologics or devices.

When reviewing research involving the use of a drug or biologic, the UIUC IRB determines whether the drug requires an IND or the investigation meets one of the FDA exemptions from the requirement to have an IND. If an IND is required, the IRB verifies the IND number prior to approving the research.
When reviewing research evaluating the safety or effectiveness of a device, the UIUC IRB determines whether the device requires an IDE, fulfills the requirements for an abbreviated IDE, or the protocol meets one of the FDA exemptions from the requirement to have an IDE. If an IDE is required, the IRB verifies the IDE number prior to approving the research. Researchers engaged in FDA regulated protocols will be required to complete the FDA Regulated Research module offered through CITI.

16.3 Procedures

16.3.1 Research Involving Medical Devices

Investigators must submit a completed IRB-1 application and related documents described therein along with Appendix B-1, Devices Form.

Initial review for IRB approval of a study involving the research-related use of a medical device may be reviewed by expedited procedures when research activities are no greater than minimal risk and (i) an IDE is not required; or (ii) the device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling. Clinical investigations for which an IDE is required are reviewed at a convened meeting.

Research with devices falls into three categories:

1. Investigations exempted from the IDE regulations;
2. Investigations of significant risk devices to determine safety and effectiveness of the device;
3. Investigations of nonsignificant risk devices to determine safety and effectiveness of the device.

When the investigator indicates on Appendix B-1 that the research is exempt from the requirement for an IDE and has not provided a letter from the FDA granting an exemption, the IRB reviews the application material and determines whether the research meets one of the FDA exemption
requirements. The IRB documents their determination in the meeting minutes, or, when the review occurs by expedited procedures, on the IRB Member Device Checklist.

16.3.1.1 FDA Categories of Exemption (Devices)

1. A device legally marketed in the US that is used or investigated in accordance with the indications in the FDA-approved labeling.

2. A diagnostic device (that is, an in vitro diagnostic device) 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.

3. 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.

4. 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.

5. 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.

6. 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 part 807 in determining substantial equivalence.

NOTE: Clinical investigations that are exempt from IDE regulations still require IRB review and approval.
16.3.1.2 Significant Risk (SR) versus Non-Significant (NSR) Risk Devices

Unless an investigational device is exempt from the requirements for an IDE, it must be categorized as either an SR device or an NSR device. The initial risk assessment is made by the sponsor.

Next, the IRB must review the sponsor’s SR or NSR assessment and modify the determination if the IRB disagrees with the sponsor. If the FDA has already made the SR or NSR determination, their determination is final and the IRB does not need to duplicate effort.

The IRB’s determination regarding the appropriate SR/NSR category must occur at a convened meeting. The determination and reason for the determination are documented in the meeting minutes. The documentation should include the SR/NSR determination letter from the FDA, if the FDA has already made a determination.

The sponsor, through the investigator, provides the IRB with the following information:

- explanation of their risk determination,
- description of device,
- reports of prior investigations,
- proposed investigational plan,
- subject selection criteria, and
- other information pertinent to the IRB deliberation.

The IRB’s risk determination should consider the device, the proposed use of the device and any protocol-related procedures (e.g., surgery). The following criteria for an SR device guide the IRB in making their determination:

a. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
b. Is for use in supporting or sustaining human life and represents a potential for serious risk to the health, safety, or welfare of a subject;

c. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or

d. Otherwise presents a potential for serious risk to a subject.

If the IRB determines that a study, submitted by the sponsor for approval as an NSR device represents an SR device, the IRB Director or Chair notifies the investigator and sponsor of this decision. The investigator will be instructed to re-submit the protocol as an SR device study and to provide documentation from the sponsor of an approved IDE (i.e., copy of the letter from the FDA providing approval or conditional approval of the IDE).

If the IRB concurs with the sponsor’s assessment of an NSR device, the IRB proceeds with its review and approval of the device study following the criteria at 21 CFR 56.111. The study may begin without submission of an IDE application to the FDA. Conduct of the NSR device study must follow the "abbreviated" requirements described at 21 CFR Sec. 812.2(b).

16.3.1.3 Significant Risk (SR) Device Research

When research is submitted for IRB review and approval as an SR device, the investigator is responsible for providing the IRB with the IDE number and a copy of the letter from the FDA providing approval or conditional approval of the IDE to confirm the validity of the IDE. The IRB Director or Chair will confirm submission of this documentation prior to IRB approval.

Initial IRB review occurs at a convened meeting.

For SR devices that are implanted, the IRB must assess the exit strategy for the device to ensure that human subjects are adequately protected once the study ends, if applicable.
16.3.1.4 Handling of Investigational Devices
The process for handling the investigational device must be provided to the IRB on Appendix B-1 for review and approval. The IRB review of the proposal includes assessing the adequacy of the device control plans. Device accountability records along with storage, dispensing and disposition of the investigational device are subject to audit by the IRB.

When the UIUC IRB serves as the IRB of record for clinical investigations of devices at other institutions, the investigator must describe the process for handling the investigational device. The IRB will seek input from a qualified individual from that institution to confirm their concurrence with the plan before approving the research.

16.3.2 Research Involving Drugs and Biologic Products
Investigators must submit a completed IRB-1 application and related documents described therein along with Appendix B-2.

Initial review for IRB approval of a study involving the research-related administration of a drug or biologic occurs at a convened IRB meeting, unless the research activities present no more than minimal risk and an IND is not required in accordance with expedited review categories.

An IND is commonly required for any clinical study that proposes the use (e.g., as a research tool to explore a biological phenomenon or disease process) or evaluation (i.e., pharmacokinetics, safety and/or effectiveness) of an unapproved drug or biological product or unapproved indication or use for a marketed drug or biologic.

If the investigator is requesting the drug or biologic (unapproved or marketed) be exempt from IND requirements, the investigator must justify this request on Appendix B-2. Alternatively, the investigator may provide the IRB with communications from the FDA indicating that an exemption from the IND regulations has been granted.

The FDA has issued a specific guidance for the use of lawfully marketed drugs and biologicals in oncology protocols. This guidance provides details and examples of those regimens that do and do not require an
IND. (Refer to FDA Guidance for Industry: IND Exemptions for Studies of Lawfully Marketed Drug or Biological Products for the Treatment of Cancer).

If the investigator has not provided an IND or letter from the FDA granting an exemption from IND requirements, the IRB reviews and determines whether the research meets one of the FDA exemption requirements below. The IRB documents their determination in the meeting minutes or, when the review occurs by expedited procedures, the IRB Member Summary Checklist.

### 16.3.2.1 Categories of Exemption (Drugs)

**Exemption 1:**

a. The drug product is lawfully marketed in the United States.

b. The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug.

c. If the drug that is undergoing investigation was lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product.

d. The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.

e. The investigation is conducted in compliance with 21 CFR 50 and 56.

f. The investigation is conducted in compliance with the requirements of 21 CFR 312.7 (Promotion and charging for investigational drugs).

A clinical investigation involving use of a placebo does not require an IND if the investigation does not otherwise require submission of an IND.

**Exemption 2:**
a. A clinical investigation involving an in vitro diagnostic biological product that meets the following:
   1. Product is blood grouping serum, reagent red blood cells, or anti-human globulin; 2. The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and 3. The diagnostic test was shipped in compliance with 21 CFR 312.160.

**Exemption 3:**
A drug intended solely for tests in vitro or in laboratory research animals if shipped in accordance with 21 CFR 312.160.

**Exemption 4:**
Clinical bioavailability or bioequivalence studies are exempt from the requirement for an IND except when one or more of the criteria described below are met:
   a. The drug product contains a new chemical entity (21 CFR 320.31(a)(1)), radioactively labeled drug product (21 CFR 320.31(a)(2)) or cytoxic product (21 CFR 320.31(a)(3)).
   b. The study involves a drug product containing an already approved, non-new chemical entity and is:
      i. A single-dose study in normal subjects or patients where either the maximum single or total daily dose exceeds that specified in the labeling of the drug product that is the subject of an approved new drug application or abbreviated new drug application; ii. A multiple-dose study in normal subjects or patients where either the single or total daily dose exceeds that specified in the labeling of the drug product that is the subject of an approved new drug application or abbreviated new drug application; or iii. A multiple-dose study on an extended release product on which no single-dose study has been completed.

**Exemption 5:**
A clinical bioavailability or bioequivalence study being conducted for approval of an abbreviated new drug application or supplemental new drug application other than studies described in 5.a. and 5.b.
above as long as samples of the reference standard and test article are retained as described in 21 CFR 320.38 and 320.63.

**NOTE:** Clinical investigations that are exempt from IND requirements still require IRB review and approval.

If the IRB determines that there may potentially be significant risk or decreased acceptability involved with the use of a drug utilizing a different route of administration, dose, or in a non-FDA approved population and/or disease, the IRB can request that the investigator contact the FDA for review of the proposed clinical investigation to determine whether the use qualifies for an exemption from the IND requirements.

The research application involving the use of a drug or biological product, unless the research is exempt from the IND regulations, must include evidence that the FDA has issued an Investigational New Drug (IND) number. The OPRS Office will confirm that the IND number provided in the IRB submission matches that recorded on the sponsor protocol, communication from the sponsor, or communication from the FDA. The Investigator's Brochure is not an acceptable mechanism for verification. Validation of the IND number is required before IRB approval.

**16.3.3 Handling of Investigational Drugs or Biologics**

If the investigator will be handling an investigational agent themselves, a process for handling it must be described on the IRB on Appendix B-2 for review and approval. The IRB may confer with the Division of Research Safety or a consultant to confirm the adequacy of the plan. Drug accountability records along with storage and dispensing of investigational drugs or biologics are subject to audit by the IRB.

When the UIUC IRB serves as the IRB record for clinical investigations of drugs and biologics at other institutions, the investigator must describe the process for handling the investigational drug. The IRB will seek input from a qualified individual from that institution to confirm their concurrence with the plan before approving the research.
16.3.4 510(k) Premarket Notification (PMN)

Any investigator considering the submission of a 510(k)/PMN may contact the OPRS Office for guidance.

The FDA must be notified 90 days in advance of intent to market a medical device.

Submission of a 510(k) to the FDA is required if there is the intention to introduce a device into commercial distribution for the first time or to reintroduce a device that will be significantly changed or modified to the extent that its safety or effectiveness could be affected. The change or amendment could relate to the design, material, chemical composition, energy source, manufacturing process, or intended use.

16.3.5 Expanded Access to Investigational Drugs and Devices

16.3.5.1 Investigational Drugs

1. Treatment IND
   a. Treatment IND [21 CFR 312.34 and 312.35] provides a mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. A treatment IND may be granted after sufficient data have been collected to show that the drug "may be effective" and does not have unreasonable risks.
   b. Four requirements must be met before a treatment IND can be issued: 1) the drug is intended to treat a serious or immediately life-threatening disease; 2) there is no satisfactory alternative treatment available; 3) the drug is already under investigation, or trials have been completed; and 4) the trial sponsor is actively pursuing marketing approval. A treatment use under a treatment IND may begin 30 days after FDA receives the protocol or on earlier notification by FDA that the treatment use described in the protocol may begin.
   c. UIUC policy is that treatment IND studies require prospective IRB review and informed consent.

2. Group C Treatment IND
The "Group C" treatment IND was established by agreement between the FDA and the National Cancer Institute (NCI). The Group C program is a means for the distribution of investigational agents to oncologists for the treatment of cancer under protocols outside the controlled clinical trial. Group C drugs are generally Phase 3 study drugs that have shown evidence of relative and reproducible efficacy in a specific tumor type. They can generally be administered by properly trained physicians without the need for specialized supportive care facilities. Group C drugs are distributed only by the National Institutes of Health under NCI protocols. Although treatment is the primary objective and patients treated under Group C guidelines are not part of a clinical trial, safety and effectiveness data are collected. The usage of a Group C drug is described in its accompanying "Guideline Protocol" document. The Guideline Protocol contains an FDA-approved informed consent document which must be used if there has been no local IRB review. UIUC policy is that Group C treatment IND studies require prospective IRB review and informed consent.

3. Parallel Track
The FDA's Parallel Track policy [57 FR 13250] permits wider access to promising new drugs for AIDS/HIV related diseases under a separate "expanded access" protocol that "parallels" the controlled clinical trials that are essential to establish the safety and effectiveness of new drugs. It provides an administrative system that expands the availability of drugs for treating AIDS/HIV. These studies require prospective IRB review and informed consent.

4. Emergency Use
For information regarding the use of Investigational Drugs for Emergency Use, please contact the OPRS Office.

16.3.5.2 Investigational Devices
1. Compassionate Use
The FDA allows the use of an unapproved device in circumstances where the device is the only option available for a patient faced with a serious or life-threatening condition that does not meet the criteria of an emergency. Prior FDA approval is required before compassionate use occurs. As a first step, the clinician should seek the approval of the IDE holder and provide them with the following information:
1. A description of the patient’s condition and circumstances necessitating,
2. A discussion of why alternative therapies are Research Involving the Use of Drugs, unsatisfactory,
3. An identification of any deviations from the approved labeling required to treat the patient, and
4. The patient protection measures that will be followed.

The IDE holder must then submit an IDE supplement to the FDA for approval. Once FDA approval is obtained, the investigator should submit the protocol including appropriate schedule for monitoring the patient, UIUC Emergency Use application form, information provided to the FDA concerning the 4 points above, informed consent document and copy of the letter from the FDA approving the IDE supplement to the IRB for review and approval. Subject should not be treated with the device until FDA and IRB approval are obtained. Following compassionate use of the device, a follow-up report should be submitted to FDA in which summary information regarding patient outcome is presented. If problems occurred as a result of device use, they should be discussed in the follow-up report. A copy of the followup report should be submitted to the UIUC IRB.

2. Treatment Use
Approved IDEs specify the maximum number of clinical sites and the maximum number of human subjects that may be enrolled in a study. During the course of a clinical trial, if the data suggest that the device is effective, then the trial may be expanded to include additional patients with life-threatening or serious diseases. To qualify for a treatment use IDE, the disease or condition must be life threatening or serious and patients must have no comparable or satisfactory alternatives to the investigational device.

FDA will consider the use of an investigational device under a treatment IDE if all of the following criteria are met:

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

Specific requirements for a treatment IDE application are available in the FDA’s guidelines on IDE Early/Expanded Access. Treatment use may begin 30 days after FDA receives the treatment IDE submission, unless FDA notifies the sponsor otherwise.

A licensed practitioner who receives an investigational device for treatment use under a treatment IDE is considered an “investigator” under FDA regulations and is responsible for meeting all applicable investigator responsibilities, including responsibilities to obtain prospective IRB approval and informed consent.

3. Continued Access to Investigational Devices

a. The sponsor of a clinical investigation is permitted to continue to enroll subjects while a marketing application is being prepared by the sponsor and/or reviewed by the Agency if there is: 1) A public health need for the device and 2) preliminary evidence that the device is likely to be effective and no significant safety concerns have been identified for the proposed indication.

b. The continued enrollment of subjects in an investigation while a marketing application is being prepared by the sponsor and/or reviewed by Office of Device Evaluation (ODE) is known as an “extended investigation.” A sponsor’s request for an extended investigation is as an IDE supplement. There is significant overlap between the treatment IDE regulation and the Continued Access Policy. The continued access policy and the treatment IDE regulation are intended to provide additional access to an unapproved device, once preliminary evidence regarding safety and effectiveness is available to FDA. However, because a treatment IDE can be submitted earlier in the IDE process, i.e., once promising evidence of safety and effectiveness has been collected under the IDE but while the clinical study is ongoing, it provides access to a wider group of patients at an earlier stage in the IDE process.

c. The treatment IDE regulation also has a more narrow application than the Continued Access Policy in that treatment use is intended to address only those patients who have an immediately
life-threatening or serious disease or condition whereas the Continued Access Policy, which is applied after completion of the clinical trial, may be considered for any clinical investigation.

4. Emergency Use
For information regarding the use of Investigational Devices for Emergency Use, please contact the OPRS Office.

5. Humanitarian Use
For information regarding the use of Investigational Devices for Humanitarian Use, please contact the OPRS Office.

16.4 Informed Consent
16.4.1 Informed Consent – General Requirements
No investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence. An informed consent checklist detailing required and additional elements has been developed. This checklist is provided to researchers as guidance when they create informed consent documents. It is also used by OPRS staff and IRB members during the review process to ensure required elements are incorporated appropriately.

16.4.2 Basic Elements of Informed Consent for FDA Regulated Research
In seeking informed consent, the following information shall be provided to each subject:
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.

2. A description of any reasonably foreseeable risks or discomforts to the subject.

3. A description of any benefits to the subject or to others which may reasonably be expected from the research.

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

5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained, and that notes the possibility that the Food and Drug Administration may inspect the records.

6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

7. An explanation of whom to contact for answers to pertinent questions about the research, the research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

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

Additional Elements of Informed Consent
When appropriate, one or more of the following elements of information shall also be provided to each subject:

9. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.
10. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

11. Any additional costs to the subject that may result from participation in the research.

12. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

13. 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.

14. The approximate number of subjects involved in the study.

15. A statement noting the possibility that the FDA may inspect the records that will be provided to each participant.

16. A statement that the results of the research will be posted on clinicaltrials.gov.
   
a. “A description of this clinical trial will be available on [http://www.ClinicalTrials.gov](http://www.ClinicalTrials.gov), as required by U.S. Law. This website will not include information that can identify you. At most the website will include a summary of the results. You can search this website at any time.

The informed consent requirements in these regulations are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed for informed consent to be legally effective.

16.4.3 Documentation of Informed Consent

Informed consent must be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117, 21 CFR 50.27 and FDA guidance documents on informed consent.

Informed consent is documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent.

A copy of the signed and dated consent form must be given to the person signing the form.

The consent form may be either of the following:
a. a written consent document that embodies the elements of informed consent may be read to
the subject or the subject's legally authorized representative, but the subject or representative
must be given adequate opportunity to read it before it is signed; or
b. a short form written consent document stating that the elements of informed consent have
been presented orally to the subject or the subject's legally authorized representative.

When this method is used:

1. there must be a witness to the oral presentation;
2. the IRB shall approve a written summary of what is to be signed by the subject or
representative;
3. the witness must sign both the short form and a copy of the summary;
4. the participant or the participant’s legally authorized representative will sign the
consent document.
5. the person actually obtaining consent must sign a copy of the summary;
6. a copy of the summary must be given to the subject or representative, in addition to a
copy of the short form;
7. for participants who do not speak English, the witness is conversant in both English and
the language of the participant;
8. the participant or the participant’s legally authorized representative will sign the
consent document.

16.4.4 Exception from Informed Consent Requirements

(a) Obtaining informed consent shall be deemed feasible unless, before use of the test article
(except as provided in paragraph (b) of this section), both the investigator and a physician who is not
otherwise participating in the clinical investigation certify in writing all of the following:

1. The human subject is confronted by a life-threatening situation necessitating the use of the
test article;
2. Informed consent cannot be obtained from the subject because of an inability to
communicate with, or obtain legally effective consent from, the subject;
3. Time is not sufficient to obtain consent from the subject's legal representative; AND
4. There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

(b) If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the subject, and time is not sufficient to obtain the independent determination required in paragraph (a) of this section in advance of using the test article, the determinations of the clinical investigator shall be made and, within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

(c) The documentation required in paragraph (a) or (b) of this section shall be submitted to the IRB within five (5) working days after the use of the test article.

16.4.5 Exception from Informed Consent Requirements for Emergency Research

Even for an emergency use, the investigator is required to obtain informed consent of the subject or the subject's legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following [21 CFR 50.23(a)]:

1. The subject is confronted by a life-threatening situation necessitating the use of the test article;
2. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
3. Time is not sufficient to obtain consent from the subject's legal representative; AND
4. 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, in the investigator's opinion, immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the clinical investigator should make the determination and, within five (5) working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. The investigator must notify the IRB within five (5) working days after the use of the test article [21 CFR 50.23(c)].
16.5 Emergency Use of a Test Article
Emergency use is defined as the use of a test article 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. Emergency use of a test article must be reported to the IRB Chair within five (5) working days. Any subsequent use of the test article at the institution is subject to IRB review.

For purposes of this section “life threatening” includes the scope of both life threatening and severely debilitating, as defined below:

Life threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life threatening do not require the condition to be immediately life threatening or to immediately result in death. Rather, the subjects must be in a lifethreatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

16.6 Recruiting Study Subjects
FDA requires that an Institutional Review Board (IRB) review and have authority to approve, require modifications in, or disapprove all research activities covered by the IRB regulations. An IRB is required to ensure that appropriate safeguards exist to protect the rights and welfare of research subjects. In fulfilling these responsibilities, an IRB is expected to review all the research documents and activities that bear directly on the rights and welfare of the subjects of proposed research. The protocol, the consent document and, for studies conducted under the Investigational New Drug (IND) regulations, the investigator’s brochure are examples of documents that the IRB should review. The IRB should also review the methods and material that investigators propose to use to recruit subjects. [21 CFR 56.109, 56.107(a), 56.111]
FDA considers direct advertising for study subjects to be the start of the informed consent and subject selection process. Advertisements should be reviewed and approved by the IRB as part of the package for initial review.

FDA expects IRBs to review the advertising to assure that it is not unduly coercive and does not promise a certainty of cure beyond what is outlined in the consent and the protocol. This is especially critical when a study may involve subjects who are likely to be vulnerable to undue influence.

When direct advertising is to be used, the IRB should review the information contained in the advertisement and the mode of its communication to determine that the procedure for recruiting subjects is not coercive and does not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol. The IRB should review the final copy of printed advertisements to evaluate the relative size of type used and other visual effects. When advertisements are to be taped for broadcast, the IRB should review the final audio/video tape.

No claims should be made, either explicitly or implicitly, that the drug, biologic or device is safe or effective for the purposes under investigation, or that the test article is known to be equivalent or superior to any other drug, biologic or device. Advertising for recruitment into investigational drug, biologic or device studies should not use terms such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational.

Advertisements should not promise "free medical treatment," when the intent is only to say subjects will not be charged for taking part in the investigation. Advertisements may state that subjects will be paid, but should not emphasize the payment or the amount to be paid, by such means as larger or bold type.

Generally, the FDA believes that 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 in advertisements:

1. the name and address of the clinical investigator and/or research facility;
2. the condition under study and/or the purpose of the research;
3. in summary form, the criteria that will be used to determine eligibility for the study;
4. a brief list of participation benefits, if any (e.g., a no-cost health examination);
5. the time or other commitment required of the subjects; and
6. the location of the research and the person or office to contact for further information

[Ref: 21 CFR 56.110; 21 CFR 50.20, 50.25, 56.111(a)(3); 56.111(b) and 812.20(b)(11); 21 CFR 312.7(a); 21 CFR 812.7(d)]

16.7 Data Retention and Subject Withdrawal in a Clinical Trial
According to FDA regulations, when a subject withdraws from a study, the data collected on the subject to the point of withdrawal remains part of the study database and may not be removed.

An investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the subject’s information.

If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous bullet, the investigator must obtain the subject’s informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). In accordance with FDA regulations, IRB approval of informed consent documents would be required. (21 CFR 50.25, 56.109(b), 312.60, 312.66, 812.100)

If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study the subject’s medical record or other confidential records requiring the subject’s consent. However, an investigator may review study data related to the subject collected prior to the
subject’s withdrawal from the study, and may consult public records such as those establishing survival status.

17 Additional Requirements for Sponsored Research

17.1 Research Funded by the Department of Defense (DOD)

17.1.1 Definitions

Research Involving a Human Being as an Experimental Subject - An activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction (32 CFR 219.102(f)) and all nonexempt classified research must be conducted following the requirements of 3216.02.13. Examples of interventions or interactions include, but are not limited to, a physical procedure, a drug, a manipulation of the subject or subject’s environment, the withholding of an intervention that would have been undertaken if not for the research purpose.

The definition of minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests” shall not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

The following shall be promptly (no longer than within 30 days) reported to the DoD human research protection officer:

- When significant changes to the research protocol are approved by the IRB.
- The results of the IRB continuing review.
- Change of reviewing IRB.
When the organization is notified by any Federal department, agency, or national organization that any part of the HRPP is under investigation for cause involving a DoD-supported research protocol.

For non-exempt research, the IRB considers the scientific merit of the research. The IRB may rely on outside experts to provide an evaluation of the scientific merit.

Records maintained that document compliance or non-compliance with DoD requirements shall be made accessible for inspection and copying by representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD component.

The IRB considers the appointment of a research monitor:

- Required for research involving greater than minimal risk, although the IRB or organizational official can require this for a portion of the research or studies involving no more than minimal risk if appropriate.
- The research monitor is appointed by name and shall be independent of the team conducting the research.
- There may be more than one research monitor (e.g., if different skills or experience are needed).
- The monitor may be an ombudsman or a member of the data safety monitoring board. The IRB must approve a written summary of the monitors’ duties, authorities, and responsibilities.
- The IRB or HRPP official shall communicate with research monitors to confirm their duties, authorities, and responsibilities.
- The duties of the research monitor are determined on the basis of specific risks or concerns about the research, such as:
  - Perform oversight functions (e.g., observe recruitment, enrollment procedures, and the consent process, oversee study interventions and interactions, review monitoring plans and unanticipated problems involving risks to participants or others, oversee data matching, data collection and analysis).
Discuss the research protocol with researchers, interview human subjects, and consult with others outside of the study.

Report observations and findings to the IRB or a designated official.

• The research monitor has the authority to:
  
  o Stop a research study in progress.  
  o Remove individuals from study.

  o Take any steps to protect the safety and well-being of participants until the IRB can assess.

The IRB determines that the disclosure includes that provisions for research-related injury follow the requirements of the DoD component.

Research involving pregnant women, prisoners, and children are subject to the DHHS Subparts B, C, and D.

• For purposes of applying Subpart B, the phrase “biomedical knowledge” shall be replaced by “generalizable knowledge.”

• The applicability of Subpart B is limited to research involving pregnant women as participants in research that is more than minimal risk and includes interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as participants.

• Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.

• Research involving prisoners cannot be reviewed by the expedited procedure.

• When the IRB reviews research involving prisoners, the prisoner representative must be present for quorum.

• In addition to allowable categories of research on prisoners in Subpart C, epidemiological research is also allowable when:

  o The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease.

  o The research presents no more than minimal risk.

  o The research presents no more than an inconvenience to the participant. If a participant becomes a prisoner, if the researcher asserts to the IRB that it is in
the best interest of the prisoner-participant to continue to participate in the research while a prisoner, the IRB chair may determine that the prisoner-participant may continue to participate until the convened IRB can review this request to approve a change in the research protocol and until the organizational official and DoD Component office review the IRB’s approval to change the research protocol. Otherwise, the IRB chair shall require that all research interactions and interventions with the prisoner-subject (including obtaining identifiable private information) cease until the convened IRB can review this request to approve a change in the research protocol. The convened IRB, upon receipt of notification that a previously enrolled human participant has become a prisoner, shall promptly re-review the research protocol to ensure that the rights and wellbeing of the human subject, now a prisoner, are not in jeopardy. The IRB should consult with a subject matter expert having the expertise of a prisoner representative if the IRB reviewing the research protocol does not have a prisoner representative. If the prisoner-participant can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner-participant’s confinement does not inhibit the ethical conduct of research, and there are no other significant issues preventing the research involving the human participants from continuing as approved, the convened IRB may approve a change in the study to allow this prisoner-participant to continue to participate in the research. This approval is limited to the individual prisoner-participant and does not allow recruitment of prisoners as participants.

- Research involving a detainee as a human participant is prohibited.
- This prohibition does not apply to research involving investigational drugs and devices when the same products would be offered to US military personnel in the same location for the same condition

Research with children cannot be exempt.
17.1.2 Research Ethics Education

For research funded by DOD initial and continuing research ethics education is a requirement for all personnel who conduct, review, approve, oversee, support, or manage human participant research. This requirement applies to the RPI, co-investigators, key research staff, and IRB members. This education is in addition to the UIUC general human subject protection training policy. The OPRS Office is responsible for communicating new initial and continuing training requirements to research personnel and IRB members.

Investigators are required to provide documentation of training to OPRS office staff when submitting an IRB application.

17.1.3 DOD Sponsored Survey Research

Surveys typically require DOD Survey Review and approval. When appropriate, the research protocol is reviewed and approved by the UIUC IRB prior to Department of Defense approval.

17.1.4 Transnational Research

When conducting DOD funded research outside of the United States the investigator must provide documentation to the IRB of permission to conduct research in that country either by certification or from the local IEB or ethics committee. The investigator must follow all local laws, regulations, customs, and practices. Additional safeguards for transnational populations may not be applicable to social and behavioral research that is determined to be no more than minimal risk.

17.1.5 Scientific Review

All substantive amendments to DOD funded research must undergo a scientific review prior to IRB review. This review shall be considered by the IRB.

17.1.6 U.S. Military Personnel as Research Participants

When research involves U.S. military personnel, additional protections to minimize undue influence are required. The researcher should address the following requirements in the IRB application:

- Officers are not permitted to influence the decision of their subordinates.
• Officers and senior non-commissioned officers may not be present at the time of recruitment.
• Officers and senior non-commissioned officers have a separate opportunity to participate.
• When recruitment involves a percentage of a unit, an independent ombudsman is present.
• When research involves U.S. military personnel, policies and procedures require limitations on dual compensation:
  i. Prohibit an individual from receiving pay from more than one position for more than 40 hours of work in one calendar week.
  ii. The policy includes temporary, part-time, and intermittent appointments.
  iii. Prohibit an individual from receiving pay of compensation for research during duty hours.
  iv. U.S. military personnel may be compensated for research if the participant is involved in research when no on duty.
  v. Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to $50 for each blood draw.
  vi. Non-Federal persons may be compensated for research participation other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.

17.1.7 Waivers of Informed Consent
If the research subject meets the definition of “experimental subject” (as defined in Section 17.1.1 above), a waiver of consent is prohibited unless a waiver is obtained from the Secretary of Defense.

If the research subject does not meet the definition of “experimental subject,” the IRB may waive consent.

17.1.8 Research Related Injury
Due to the possibility of injuries arising from participation in human subject research, every project involving greater than minimal risk shall include an arrangement for emergency treatment and necessary follow-up of any research-related injury. The IRB will determine whether any treatment or
follow-up plan is required for research involving minimal risk. This plan shall be disclosed in the informed consent document.

17.1.9 Prohibition of Research with Prisoners of War (POW) and Detainees
Research involving any person captured, detained, held or otherwise under the control of DOD personnel (military and civilian, or contractor employee) is prohibited. Investigators and the IRB should refer to the definition of “prisoner of war” for the particular Department of Defense component supporting the research.

17.1.10 Multi-Site Research
When conducting multi-site research, a formal agreement between organizations is required to specify the roles and responsibilities of each party. UIUC policies as described in section 4.3 also apply.

[References: 32 CFR 219; SECNAVYINST 3900.39D; Department of Defense Directive 3216.2; OPAVINST 5300.8C]

17.2 Research Sponsored by the National Institute of Justice
In addition to the standard IRB review process, additional requirements are placed on research funded by the National Institute of Justice (NIJ). (28 CFR 22; 28 CFR 512)

17.2.1 Privacy Certificate
Researchers with NIJ funded projects are required to have a Privacy Certificate approved by the NIJ Human Subjects Protection Officer. The Privacy Certificate assures that the researcher understands the responsibilities to protect the confidentiality of research and statistical information and has developed specific procedures to ensure that this information is only used or revealed in accordance with the requirements of federal regulations. Under a privacy certificate, researchers and research staff do not have to report child abuse unless the participant signs another consent form to allow child abuse reporting. Information about Privacy Certificates may be found at the NIJ website information on Human Subjects and Privacy Protection.
17.2.2 Confidentiality Statements
In accordance with 28 CFR 22 for NIJ funded research, investigators and research staff are required to sign Employee Confidentiality Statements, which are maintained by the responsible investigator. A Model Employee Confidentiality Statement can be found on the NIJ website. The confidentiality statement on the consent form must state that confidentiality can only be broken if the participant reports immediate harm to participants or others.

17.2.3 Research Conducted within the Bureau of Prisons
Additional requirements for prospective researchers to obtain approval to conduct research within the Bureau of Prisons (Bureau) are described at CFR 512. Although some research may be exempt from 28 CFR part 46 under §46.101(b)(5), as determined by the Office of Research and Evaluation (ORE) of the Bureau, no research is exempt from 28 CFR part 512. However, implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research. The researcher must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor to the researcher. For research conducted within the Bureau of Prisons, the organization, IRB, and researchers and research staff must follow the requirements of 28 CFR 512, including:

- All research proposals will be reviewed by the Bureau Research Review Board.

17.2.3.1 Requirements for Research Projects and Researchers
For research conducted within the Bureau of Prisons, the UIUC IRB, investigators, and research staff must follow the requirements of 28 CFR 512, including:

1. In all research projects the rights, health, and human dignity of individuals involved must be respected.
2. The project must have an adequate research design and contribute to the advancement of knowledge about corrections.
3. The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.
4. The project must minimize risk to subjects; risks to subjects must be reasonable in relation to anticipated benefits. The selection of subjects within any one institution must be equitable.
When applicable, informed consent must be sought and documented.

5. Incentives may not be offered to help persuade inmate subjects to participate. However, soft drinks and snacks to be consumed at the test setting may be offered. Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research subjects who are both:
   a. No longer in Bureau of Prisons custody, and
   b. Participating in authorized research being conducted by Bureau employees or contractors.

6. The researcher must have academic preparation or experience in the area of study of the proposed research.

7. The researcher must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor to the researcher.

8. Except as noted in the informed consent statement to the subject, the researcher must not provide research information which identifies a subject to any person without that subject's prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertains.

9. The researcher must adhere to applicable provisions of the Privacy Act of 1974 and regulations pursuant to this Act.

10. The research design must be compatible with both the operation of prison facilities and protection of human subjects. The researcher must observe the rules of the institution or office in which the research is conducted.

11. Any researcher who is a non-employee of the Bureau must sign a statement in which the researcher agrees to adhere to the provisions of this subpart.

12. Except for computerized data records maintained at an official Department of Justice site, records which contain nondisclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system.

13. If the researcher is conducting a study of special interest to the Office of Research and
Evaluation (ORE), but the study is not a joint project involving ORE, the researcher may be asked to provide ORE with the computerized research data, not identifiable to individual subjects, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.

14. The researcher must submit planned methodological changes in a research project to the IRB for approval, and may be required to revise study procedures in accordance with the new methodology.

17.2.3.2 Research Proposals

When submitting a research proposal, the investigator shall provide the following information:

1. A summary statement which includes:
   a. Name(s) and current affiliation(s) of the researcher(s);
   b. Title of the study;
   c. Title of the study;
   d. Purpose of the project;
   e. Location of the project;
   f. Methods to be employed;
   g. Anticipated results;
   h. Duration of the study;
   i. Number of subjects (staff/inmates) required and amount of time required from each; and
   j. Indication of risk or discomfort involved as a result of participation.

2. A comprehensive statement which includes:
   a. Review of related literature;
   b. Detailed description of the research method;
   c. Significance of anticipated results and their contribution to the advancement of knowledge;
   d. Specific resources required from the Bureau;
   e. Description of all possible risks, discomforts, and benefits to individual subjects or a class of subjects, and a discussion of the likelihood that the risks and discomforts will actually occur;
f. Description of steps taken to minimize any risks.

g. Description of physical and/or administrative procedures to be followed to: (i) Ensure the security of any individually identifiable data that are being collected for the project, and (ii) Destroy research records or remove individual identifiers from those records when the research has been completed.

h. Description of any anticipated effects of the research project on institutional programs and operations; and

i. Relevant research materials such as vitae, endorsements, sample informed consent statements, questionnaires, and interview schedules.

j. A statement regarding assurances and certification required by 28 CFR part 46, if applicable.

17.2.3.3 Informed Consent

Before commencing a research project requiring participation by staff or inmates, the researcher shall give each participant a written informed consent statement containing the following information:

1. Identification of the principal investigator(s);

2. Objectives of the research project;

3. Procedures to be followed in the conduct of research;

4. Purpose of each procedure;

5. Anticipated uses of the results of the research;

6. A statement of benefits reasonably to be expected;

7. A declaration concerning discomfort and risk, including a description of anticipated discomfort and risk;

8. A statement that participation is completely voluntary and that the participant may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable);

9. A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, a researcher may not guarantee confidentiality when the subject indicates an intent to commit future criminal
conduct or harm himself/herself or someone else, or, if the subject is an inmate, indicates an intent to leave the facility without authorization. Under the privacy certificate investigators and research staff do not have to report child abuse unless the participant signs another consent form to allow child abuse reporting;

10. A statement that participation in the research project will have no effect on the inmate participant's release date or parole eligibility;

11. An offer to answer questions about the research project; and

12. Appropriate additional information as needed to describe adequately the nature and risks of the research.

A researcher who is a non-employee of the Bureau, in addition to presenting the statement of informed consent to the subject, shall also obtain the subject's signature on the statement of informed consent prior to initiating the research activity. The researcher may not be required to obtain the signature if the researcher can demonstrate that the only link to the subject's identity is the signed statement of informed consent or that there is significantly more risk to the subject if the statement is signed. The signed statement shall be submitted to the chairperson of the appropriate local research review board.

17.2.3.4 **Access to Bureau of Prisons Records**

A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency.

Except as noted in the informed consent statement to the subject, the researcher must not provide research information which identifies a subject to any person without that subject's prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertains.
17.2.3.5 Reports and Publications
The researcher shall prepare reports of progress on the research and at least one report of findings. At least once a year, the researcher shall provide the Chief, ORE, with a report on the progress of the research. At least 12 working days before any report of findings is to be released, the researcher shall distribute one copy of the report to each of the following: the chairperson of the BRRB, the regional director, and the warden of each institution which provided data or assistance. The researcher shall include an abstract in the report of findings.

A researcher may publish in book form and professional journals the results of any research project. In any publication of results, the researcher shall acknowledge the Bureau's participation in the research project. The researcher shall expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.

Prior to submitting for publication the results of a research project conducted under this subpart, the researcher shall provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.

For all NIJ-funded research, a copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, or other relevant research materials.

17.3 Research Sponsored by the Department of Education and Family Educational Rights and Privacy Act (FERPA)
In addition to the Policies and Procedures described above, research sponsored by the Department of Education is subject to additional regulations.

For research not funded by the U.S. Department of Education: The IRB must verify compliance with U.S. Department of Education regulations that schools are required to develop and adopt policies in conjunction with parents regarding the following:

- Any applicable procedures for granting a request by a parent for reasonable access to such survey within a reasonable period of time after the request is received.
• Any applicable procedures for granting a request by a parent for reasonable access to instructional material received.

• The collection, disclosure, or use of personal information collected from students for the purpose of marketing or for selling that information (or otherwise providing that information to others for that purpose), including arrangements to protect student privacy that are provided by the agency in the event of such collection, disclosure, or use.

• The right of a parent of a student to inspect, upon the request of the parent, any instrument used in the collection of personal information before the instrument is administered or distributed to a student.

• Any applicable procedures for granting a request by a parent for reasonable access to such instruments within a reasonable period of time after the request is received.

17.3.1 Family Educational Rights and Privacy Act (FERPA) 34 CFR Part 99
The Family Educational Rights and Privacy Act is a Federal law that protects the privacy of student education records. In general, schools must have written permission from the parent or eligible student in order to release any information from a student's education record. However, FERPA allows schools to disclose personally identifiable information from an education record of a student without consent if the disclosure is to organizations conducting studies for, or on behalf of, educational agencies or institutions to:

1. Develop, validate, or administer predictive tests;
2. Administer student aid programs; or
3. Improve instruction.

17.3.2 Exception to Written Permission for Records Release under FERPA
At UIUC the exception to written permission from the parent or student for records release is generally managed by the Office of School and University Research Relations (OSURR) in the College of Education or may be delegated to the IRB. A school district or postsecondary institution that uses this exception is
required to enter into a written agreement with the University or with the investigator conducting the research that specifies:

- The determination of the exception.
- The purpose, scope, and duration of the study.
- The information to be disclosed.
- That information from education records may only be used to meet the purposes of the study stated in the written agreement and must contain the current requirements in 34 CFR 99.31(a) (6) on re-disclosure and destruction of information.
- That the study will be conducted in a manner that does not permit personal identification of parents and students by anyone other than representatives of the university with legitimate interests.
- That the University is required to destroy or return all personally identifiable information when no longer needed for the purposes of the study.
- The time period during which the university must either destroy or return the information.

Education records may be released without consent under FERPA if all personally identifiable information has been removed including:

- Student’s name and other direct personal identifiers, such as the student’s social security number or student number.
- Indirect identifiers, such as the name of the student’s parent or other family members; the student’s or family’s address, and personal characteristics or other information that would make the student’s identity easily traceable; date and place of birth and mother’s maiden name.
- Biometric records, including one or more measurable biological or behavioral characteristics that can be used for automated recognition of an individual, including fingerprints, retina and iris patterns, voiceprints, DNA sequence, facial characteristics, and handwriting.
- Other information that, alone or in combination, is linked or linkable to a specific student that would allow a reasonable person in the school community, who does not have personal knowledge of the relevant circumstances, to identify the student with reasonable certainty.
17.3.3 Protection of Pupil Rights Amendment PRPA (34 CFR Part 98)

Research funded by the Department of Education must comply with additional protections under PRPA 34 CFR Part 98. No student shall be required, as part of any research project, to submit without prior consent to surveys, psychiatric examination, testing, or treatment, or psychological examination, testing, or treatment, in which the primary purpose is to reveal information concerning one or more of the following:

1. Political affiliations.
2. Mental and psychological problems potentially embarrassing to the student or his or her family.
3. Sex behavior and attitudes.
4. Illegal, anti-social, self-incriminating and demeaning behavior.
5. Critical appraisals of other individuals with whom the student has close family relationships.
6. Legally recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers.
7. Religious practices, affiliations, or beliefs of the student or student’s parent.
8. Income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under a program.

As used above, prior consent means:

1. Prior consent of the student, if the student is an adult or emancipated minor; or
2. Prior written consent of the parent or guardian, if the student is an un-emancipated minor.

Schools and contractors obtain prior written parental consent before minor students are required to participate in any ED-funded survey, analysis, or evaluation.

17.3.4 Access to Instructional Material Used in a Research or Experimentation Program Under PRPA

All instructional material—including teachers’ manuals, films, tapes, or other supplementary instructional material—which will be used in connection with any research or experimentation program...
or project shall be available for inspection by the parents or guardians of the children engaged in such program or project.

As used above:

Research or experimentation program or project means any program or project in any program under in any research that is designed to explore or develop new or unproven teaching methods or techniques.

Children means persons not above age 18 who are enrolled in research not above the elementary or secondary education level, as determined under state law where the research is taking place.

17.3.5 Additional Requirements for School Research Not Funded by the US Department of Education

The IRB must verify compliance with U.S. Department of Education regulations that schools are required to develop and adopt policies in conjunction with parents regarding the following:

- The right of parents to inspect, upon request, a survey created by a third party before the survey is administered or distributed by a school to students.
- Arrangements to protect student privacy in the event of the administration of a survey to students, including the right of parents to inspect, upon request, the survey, if the survey contains one or more of the same eight items of information noted above.
- The right of parents to inspect, upon request, any instructional material used as part of the educational curriculum for students.
- The administration of physical examinations or screenings that the school may administer to students.

17.3.6 Other Conditions Pertaining to Waivers of Parent Permission or Informed Consent

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 9.3 above [45 CFR 46.116(d)(1-4)] and if the IRB determines that the research protocol is designed for conditions or a subject population
for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children).

- 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 law. 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.

17.3.7 Additional Criteria for IRB Membership for Research Funded by National Institute on Disability and Rehabilitation Research

When children with disabilities or persons with mental disabilities are purposefully included as research subjects, the Institutional Review Board's membership must include at least one person who is primarily concerned with the welfare of these research subjects [34 CFR 350.4(c) and 356.3(c)].

[Reference: 34 CFR 97; 34 CFR 98; 34 CFR 99; 34 CFR 350; 34 CFR 356; 45 CFR 46.116(d); 45 CFR 46.401 (Subpart D)]

17.4 Research Funded by the Environmental Protection Agency

In addition to the standard IRB review and approval process additional requirements are placed on research funded by the Environmental Protection Agency. (See 40 CFR 26; 40 CFR 26.201-203; 40 CFR 26.304; 40 CFR 26.404-405)

17.4.1 Definitions

Child means a person who has not attained the age of 18 years.

Administrator means the Administrator of the Environmental Protection Agency and any other officer or employee of the Environmental Protection Agency to whom authority has been delegated by the Administrator.

Assent means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.
Permission means the agreement of parent(s) or guardian to the participation of their child or ward in research.

Parent means a child's biological or adoptive parent.

Guardian means an individual who is authorized under applicable State, Tribal, or local law to consent on behalf of a child to general medical care.

Research involving intentional exposure of a human subject means a study of a substance in which the exposure to the substance experienced by a human subject participating in the study would not have occurred but for the human subject's participation in the study.

Observational research means any research with human subjects that does not meet the definition of research involving intentional exposure of a human subject in §26.202(a).

Minimal 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.

17.4.2 Research Involving Intentional Exposure of Any Human Subject
The EPA does not conduct or support research involving intentional exposure of any human subject who is a pregnant woman (and therefore her fetus), a nursing woman, or a child.

17.4.3 Observational Research Involving Pregnant Women and Fetuses
Observational research involving pregnant women or fetuses is allowable if the IRB determines that all conditions met under section 10.2.2 above are met.

17.4.4 Observational Research of Children Not Involving Greater Than Minimal Risk
Observational research not involving greater than minimal risk is allowable only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians. (See 10.1.3.1 above.)
17.4.5 Observational Research of Children Involving Greater than Minimal Risk
Observational research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects is allowable only if the IRB finds that:

a. The intervention or procedure holds out the prospect of direct benefit to the individual subject or is likely to contribute to the subject's well-being;

b. The risk is justified by the anticipated benefit to the subjects;

c. 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

d. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

17.4.6 Final Review by EPA
EPA policy requires submission of IRB determinations and approval to the EPA Human Subjects Research Review official for final review and approval before the research can begin.

17.4.7 Research Not Conducted or Supported By Any Federal Agency
For research not conducted or supported by any federal agency that has regulations for protecting human research participants and for which the intention of the research is submission to the EPA, the EPA regulations protecting human research participants apply, including:

- EPA extends the provisions of the 40 CFR 26 to human research involving the intentional exposure of non-pregnant, non-nursing adults to any substance.
- EPA prohibits the intentional exposure of pregnant women, nursing women, or children to any substance.