

OFFICE OF HUMAN RESEARCH ETHICS  
THE UNIVERSITY OF NORTH CAROLINA  
AT CHAPEL HILL

RESEARCHER'S GUIDE  
TO THE  
IRB PROCESS  
AND  
HUMAN SUBJECTS RESEARCH

# TABLE OF CONTENTS

1.	Introduction to the Human Research Protection Program, a Shared Responsibility...	3
2.	Contact Information and Useful Links .....	4
	At the University of North Carolina at Chapel Hill.....	4
	External to the University.....	4
3.	The Core Requirements of Human Subjects Research.....	5
4.	Researcher Responsibilities .....	6
	Principal Investigator (PI).....	6
	Trainee Investigator (TI).....	6
	All Research Team Members.....	6
5.	Ethical and Regulatory Bases for Human Subjects Research.....	7
	The Belmont Report.....	7
	DHHS Office of Human Research Protections (OHRP) Regulations .....	7
	DHHS Food and Drug Administration (FDA) Regulations.....	8
6.	Does the Study Require IRB Review? .....	9
	Is the Study Human Subjects Research at UNC-Chapel Hill?.....	9
	Is it Research? .....	9
	Does it Involve Human Subjects? .....	9
	Is it Conducted Under the Aegis of UNC Chapel Hill?.....	10
7.	Applying for Initial IRB Review .....	11
8.	The IRB Review Process .....	12
	Overview of the IRB Review Process.....	12
	IRB Determinations.....	12
9.	Factors in IRB Evaluation .....	14
	Risk .....	14
	Benefit.....	14
10.	Major Investigator Responsibilities after IRB Initial Approval .....	16
	Informed Consent – A Process.....	16
	Reporting Adverse Events and Unexpected Problems in Human Subjects Research.....	17
	IRB Approval Required for All Modifications and Amendments to Previously Approved Protocols.....	18
11.	Additional Guidance on Specific Topics.....	21

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## 1. INTRODUCTION TO THE HUMAN RESEARCH PROTECTION PROGRAM, A SHARED RESPONSIBILITY

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**It is a privilege and not a right to conduct research with human subjects.** Whether the research is social, behavioral or biomedical, responsible conduct of human subjects research requires commitment and expertise in the protection of human subjects rights and welfare in addition to the expertise of an investigator's scholarly discipline. The purpose of this guide is to assist investigators in meeting their obligations by providing a reference guide to the ethical principles, federal regulations and campus review processes for human subjects research at the University of North Carolina at Chapel Hill.

We are all partners in the UNC-Chapel Hill Human Research Protection Program protecting the rights and welfare of human research subjects and the integrity of the human subjects research enterprise.

This manual contains some sections useful to all campus human subjects research investigators and other material that addresses issues specific to only a subset of research studies. Issues, regulations and campus procedures in human subjects research evolve over time, as will this guide. If you have suggestions for improvement of the guide, please share your constructive thoughts with the Office of Human Research Ethics, which will maintain and update this guide. You will also find supplemental information at the OHRE web, [ohre.unc.edu](http://ohre.unc.edu).

Please review and familiarize yourself with the manual. Refer to the guide in preparing your application for Institutional Review Board review of your human subjects research protocol. If you are daunted by the amount of material in this manual and are postponing your review, at a minimum review the five core requirements in Section 3. Researchers who consider themselves experienced practitioners of ethical human subjects research have been known to jeopardize all human subjects research at their institution by failing to comply with one or more of these requirements.

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## 2. CONTACT INFORMATION AND USEFUL LINKS

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### AT THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL

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(919) 966-3685

#### INSTITUTIONAL REVIEW BOARDS

Behavioral: (919) 962-7761  
Biomedical: (919) 966-1344  
Dental: (919) 966-1165  
Nursing: (919) 966-8520  
Public Health: (919) 966-9347

IRB contact information is maintained at [ohre.unc.edu/contact.php](http://ohre.unc.edu/contact.php)

#### INSTITUTIONAL OFFICIAL

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Vice Chancellor for Research and Economic Development  
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#### EXTERNAL TO THE UNIVERSITY

DHHS Office of Human Research Protections (OHRP): [www.hhs.gov/ohrp/about/](http://www.hhs.gov/ohrp/about/)  
OHRP guidance documents: [www.hhs.gov/ohrp/policy/index.html](http://www.hhs.gov/ohrp/policy/index.html)  
OHRP compliance references: [www.hhs.gov/ohrp/compliance/](http://www.hhs.gov/ohrp/compliance/)

DHHS Food and Drug Administration (FDA): [www.fda.gov/](http://www.fda.gov/)  
FDA guidance documents: [www.fda.gov/opacom/morechoices/industry/guidedc.htm](http://www.fda.gov/opacom/morechoices/industry/guidedc.htm)  
FDA compliance references: [www.fda.gov/ora/compliance\\_ref/](http://www.fda.gov/ora/compliance_ref/)

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### 3. THE CORE REQUIREMENTS OF HUMAN SUBJECTS RESEARCH

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1. University of North Carolina at Chapel Hill research may not involve human subjects prior to UNC-Chapel Hill IRB review and approval of the research study.
2. Changes to IRB-approved human subjects research protocols or instruments may not be implemented without prior UNC-Chapel Hill IRB approval of the changes.
3. Informed consent is a process, not a document, and is central to ethical involvement of human subjects in research. Investigators should be forthright and realistic in describing the benefits and drawbacks of participation in a human subject research protocol, and in answering all questions posed by human subjects.
4. Investigators and research team members should do their best to adhere to the protocol which the IRB approves; however, when deviations or violations occur, they should be prompt in reporting them to the IRB.
5. Adverse events and unexpected problems must be reported in accord with IRB policy.

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#### 4. RESEARCHER RESPONSIBILITIES

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##### PRINCIPAL INVESTIGATOR (PI)

The principal investigator is the individual responsible for the performance of the research study, and, as such, must personally conduct or supervise the research. The PI is responsible for ensuring that the research study is accurately and completely submitted for IRB review; that IRB approval is obtained prior to initiation of research or before making any changes or additions to the research; that the IRB is informed of all changes in information previously presented to the IRB; that progress reports are submitted to the IRB as required; and that all unanticipated problems or serious adverse events involving risk to human subjects are reported to the IRB. The PI is also responsible for ensuring that all members of the research team comply with the findings, determinations, and requirements of the IRB, including satisfactory performance of the informed consent process.

##### TRAINEE INVESTIGATOR (TI)

A trainee investigator is a student, employee in a postdoctoral training program, or a fellow who has a leadership role in a research study but who may not qualify to be named the PI for a project according to University policy. A trainee investigator may conduct the majority of the research for a given protocol, but does not have ultimate administrative and fiscal responsibility for the project. The ultimate responsibility remains with the PI.

##### ALL RESEARCH TEAM MEMBERS

The research team includes everyone engaged in the design, conduct or analysis of the study, which means not only the Principal Investigator and co-investigators but also research assistants, study coordinators, clinical research coordinators, clinical research associates, etc. Every member of the research team is responsible for protecting human subjects in accordance with the guidelines specified above, and for complying with all IRB findings, determinations and requirements. All research team members must complete human subjects research training as required by the University's "[Policy on Education and Certification of Investigators Involved in Human Subjects Research](#)."

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**5. ETHICAL AND REGULATORY BASES FOR HUMAN SUBJECTS RESEARCH  
AT UNC-CHAPEL HILL**

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UNC-Chapel Hill has an agreement with the federal government (“Federal Wide Assurance”) covering all human subjects research at UNC-Chapel Hill, without regard for sponsorship or federal involvement. In its Federal Wide Assurance, UNC-Chapel Hill pledges that all of its human subjects research will be performed in accord with the ethical principles of the [Belmont Report](#) as well as the requirements of federal regulations governing human subjects research, [45 CFR 46](#) and [21 CFR 50](#) and [56](#), which prescribe the Institutional Review Board (“IRB”) procedures.

**THE BELMONT REPORT**

“The [Belmont Report](#)” is the title of the report on “Ethical Principles and Guidelines for the Protection of Human Subjects of Research” issued on April 18, 1979 by the U.S. Department of Health, Education and Welfare from The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. This statement of ethical principles for human subjects research is the foundation for federal regulations that followed. The Belmont Report elucidates three key ethical principles in human subjects research:

- Respect for persons (applied by obtaining informed consent, consideration of privacy, confidentiality, and additional protections for vulnerable populations);
- Beneficence (applied by weighing risks and benefits);
- Justice (applied by the equitable selection of subjects).

**DHHS OFFICE OF HUMAN RESEARCH PROTECTIONS (OHRP) REGULATIONS**

**45 CFR 46: PROTECTION OF HUMAN SUBJECTS**

[45 CFR 46](#), published by the Department of Health and Human Services, codifies basic human subject protection measures. It applies to all human subjects research at UNC-CH, including the subset that is also subject to FDA regulations. 45 CFR 46 is often called The Common Rule because it has been adopted by many – though not all – federal agencies that sponsor human subjects research. Here are the federal agencies that have adopted 45 CFR 46 as the regulation for human subjects research they sponsor:

US Department of Agriculture	Department of Housing and Urban Development
Department of Energy	Department of Justice
National Aeronautics and Space Administration	Department of Defense
Department of Commerce	Department of Education
Consumer Product Safety Commission	Department of Veteran’s Affairs
International Development Cooperation Agency	Environmental Protection Agency
Agency for International Development	Department of Health and Human Services
	National Science Foundation
	Department of Transportation

**DHHS FOOD AND DRUG ADMINISTRATION (FDA) REGULATIONS**

PROTECTION OF HUMAN SUBJECTS: 21 CFR 50

[www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=50](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=50)

INSTITUTIONAL REVIEW BOARDS: 21 CFR 56

[www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=56](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=56)

INVESTIGATIONAL NEW DRUG APPLICATION: 21 CFR 312

[www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=312](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=312)

INVESTIGATIONAL DEVICE EXEMPTIONS: 21 CFR 812

[www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=812](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=812)

These FDA Regulations - 21 CFR 50, 21 CFR 56, 21 CFR 312, 21 CFR 812 - include most of the human subjects protection regulations specified by the FDA for research subject to FDA oversight. Many FDA regulations mirror the provisions in 45 CFR 46; however, they also include other provisions that address circumstances specific to research including test articles subject to FDA regulations and they address data and documentation procedures required of studies supporting an application for FDA approval.

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## 6. DOES THE STUDY REQUIRE IRB REVIEW?

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### IS THE STUDY HUMAN SUBJECTS RESEARCH AT UNC-CHAPEL HILL?

The IRB has been charged with the responsibility for reviewing and monitoring human subjects research conducted under the aegis of UNC-Chapel Hill. Therefore, the first question with respect to IRB review of a project is a determination of whether the project fits this definition. In light of the mission to protect human subjects and the potential regulatory consequences of not providing IRB review of a study later determined to have required IRB review under federal regulation, the investigator should choose to err on the side of consulting the IRB when the investigator is uncertain whether the study is human subjects research. The federal Office of Human Research Protections has a decision chart to assist in determining whether research is human subjects research [www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm](http://www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm) select: [Chart 1](#): Is an Activity Research Involving Human Subjects?

### IS IT RESEARCH?

Federal Regulations define research as “a systematic investigation, including development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for the purposes of this policy, whether or not they are supported under a program which is considered research for other purposes.” (45 CFR 46.102(d)) As described in the Belmont Report “...the term 'research' designates an activity designed to test an hypothesis [and] permit conclusions to be drawn... Research is usually described in a formal protocol that sets forth an objective and a set of procedures to reach that objective.”

Thus, a key aspect of research is that there be a systematic design in advance, generally utilizing a scientific approach or protocol, for the defined purpose of contributing to generalizable knowledge. Research can include a wide variety of activities including: experiments, observational studies, surveys, tests, and recordings. Studies assigned an Investigational New Drug (IND) number or an Investigational Device Exemption (IDE) by the FDA are, by definition, research that requires IRB review. (21 CFR 56.103)

“Research” generally does **not** include such operational activities as: defined practice activities in public health, medicine, psychology, and social work (e.g., routine outbreak investigations and disease monitoring in public health); studies for internal management purposes such as program evaluation, quality assurance, quality improvement, fiscal or program audits, or marketing studies. It generally does not include journalism or political polls. However, some of these activities may include or constitute research in circumstances where there is clear advance interest to contribute to generalizable knowledge with a scientific protocol. An intent to publish is just one possible indication of an intent to contribute to generalizable knowledge.

### DOES IT INVOLVE HUMAN SUBJECTS?

A human subject is defined by Federal Regulations as “a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.” (45 CFR 46.102(f)(1),(2)) Identifiable private information “includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation is taking place,” (such as a public restroom) “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 health care record).” (45 CFR 46.102(f)(2))

Although there is no definition of “identifiable” information in the Common Rule, “identifiable” means the information contains one or more data elements that can be combined with other reasonably available information to identify an individual.

Intervention includes physical procedures, manipulations of the subject or manipulations of the subject's environment for research purposes. Interaction includes communication between the investigator and the subject. This includes face-to-face, mail and phone interaction as well as any other mode of communication. Private information includes observation of behavior when an individual can reasonably expect that no observation is taking place, or information for specific purposes (such as a health care record) that individuals can reasonably expect will not be made public. Thus, approaches involving only existing records or human specimens or observations may still constitute human subjects research requiring IRB approval. The IRB will make this determination. Simple observational studies of public behavior (including television and internet chat rooms) do not involve human subjects as defined, because there is no intervention or interaction and the behavior is not private. Also, studies based on data collected for non-research purposes may not constitute human subjects research if individual identity is not identifiable. Examples include programmatic data such as service statistics, school attendance data, crime statistics, or election returns. Studies based on data that are individually identifiable data but also are publicly available may not constitute human subjects research [45 CFR 46.101(b)(4)]; however, the term “publicly available” is intended to refer to record sets that are truly readily available to the broad public, such as death certificates. An investigator should not assume information qualifies as “publicly available” in this context merely because it has been posted on an electronic website somewhere and can be accessed without authorization.

#### **IS IT CONDUCTED UNDER THE AEGIS OF UNC CHAPEL HILL?**

In the interests of protecting human subjects participating in research that would appear to be under university control, human subjects research that meets any of the following criteria is subject to UNC-Chapel Hill IRB review and monitoring:

- Research sponsored by UNC-Chapel Hill or performed pursuant to a contract to which UNC-Chapel Hill is a party; or
- Research conducted or directed by any employee or trainee of the university in connection with his or her UNC-Chapel Hill responsibilities; or
- Research involving access to any property or facility of UNC-Chapel Hill other than access to open spaces on the University campus that are readily available to the public at large.

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## 7. APPLYING FOR INITIAL IRB REVIEW

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Every application for initial IRB review must contain the OHRE IRB [Application for IRB Approval of Human Subjects Research](#) plus whichever of the following materials are relevant to the study:

- Study protocol: investigator’s protocol, master protocol, industry sponsor’s protocol, etc.
- Consent and assent forms, fact or information sheets; include phone consent scripts, third-party scripts (e.g., permission to turn over names to PI)
- Investigator Brochure, if a drug study
- All recruitment materials including third-party scripts, flyers and advertising, letters, emails
- Questionnaires, interview scripts, phone scripts, etc.
- Focus group guides
- Data use agreements (for approved use of existing data from third parties)
- Documentation of approvals from any other reviewing bodies (e.g., department committees, GCRC, etc)
- Documentation of training in research ethics
- Extramural grant application (e.g., NIH, foundation, etc)

See the instructions included with the [Application for IRB Approval of Human Subjects Research](#) for other items that might be required for some studies.

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## 8. THE IRB REVIEW PROCESS

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### OVERVIEW OF THE IRB REVIEW PROCESS

The OHRE will conduct an initial screening of all IRB applications for completeness and make a preliminary determination of the type of review to be conducted. Protocols submitted to the IRB are:

- reviewed by the convened IRB; or
- reviewed in an expedited fashion and assessed by the IRB; or
- reviewed and deemed exempt from continuing IRB review.

In order to determine the type of review necessary, the IRB chair or his/her designee screens the entire application and makes determinations as to whether the project constitutes human subjects research and, if so, the type of review required. It is the prerogative and responsibility of the IRB chair or designee to make the ultimate determination of whether or not a human subjects study is exempt from continuing review and well as determination of the type of review for studies not deemed exempt. All applications are assigned to review at a convened meeting unless they meet the criteria for expedited review or exemption.

Any study involving greater than minimal risk requires a review by the convened IRB. A few examples of studies typically involving greater than minimal risk:

- Studies involving vulnerable populations including pregnant women, prisoners, mentally incompetent patients, etc.
- Any clinical interventional study that randomly assigns human subjects to alternative experimental or placebo groups
- Studies involving sensitive information connected to personal identifiers

These are examples rather than guidelines; all decisions concerning review type will be made on a case-by-case basis.

### IRB DETERMINATIONS

#### EXEMPTION FROM CONTINUING REVIEW

If the IRB determines that a project is exempt from continuing review, the investigator will be so notified. The project can go forward and the investigator does not need to notify the IRB unless he or she wishes to amend the study.

#### APPROVAL OF RESEARCH

In the case of an approval with no changes, the research may proceed once the PI receives written documentation of IRB approval.

Unless otherwise specified, the approval period for research approved without changes is one year from the date of the meeting at which approval was granted.

#### STIPULATED CHANGES REQUIRED PRIOR TO APPROVAL

The IRB may determine s that a study may be approved with stipulated minor changes. Minor changes are those changes that do not involve potential for increased risk or decreased benefit to the human subjects. Some examples of minor changes are: changes in contact information or identity of non-key research personnel, changes in the study title, and changes in the consent form that reflect the minor changes listed earlier.

#### DEFERRAL

The term “deferral” is used to describe the situation in which an IRB determines that substantive changes must be made to the protocol. On occasion, the IRB requires substantive changes before approval can be granted for the research protocol. The PI’s response, including any amended materials, must be reviewed by the convened IRB.

Subject to IRB discretion, a proposal may be withdrawn if the PI does not respond to a deferral within a reasonable amount of time.

#### DISAPPROVAL

If the IRB determines that the research cannot be conducted at UNC-Chapel Hill or by employees or agents of the University or otherwise under the auspices of the University, the project, as proposed, is disapproved and may not go forward.

Disapproval usually indicates that a proposal requires major changes not likely to be feasible without a complete investigator reassessment of the protocol.

#### SUSPENSION OR TERMINATION OF RESEARCH STUDY BY IRB

The chair of the IRB or the convened IRB may suspend a study at any time if one or the other party determines that the study requires further review or evaluation. This determination may be made due to an adverse event, noncompliance or other danger to human subjects. If a project is suspended, research (including all contact with subjects not required to ensure subject safety) must immediately cease.

#### NOTIFICATION OF IRB ACTIONS

The IRB sends written notification of actions taken to the PI. If revisions to new and continuing human subjects applications are required, correspondence is sent to the investigator detailing requests for revisions, clarification, or additional information as well as information regarding continuing review.

#### APPEAL OF IRB DECISIONS

Investigators may appeal the IRB requirement for specific changes in the protocol and/or consent document(s). At the discretion of the chair, the investigator may make such an appeal in writing to the IRB. At the IRB’s discretion, the PI may be invited to the IRB meeting at which his or her case will be discussed.

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## 9. FACTORS IN IRB EVALUATION

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For more detailed discussion of these factors, please see the UNC-Chapel Hill IRB Standard Operating Procedures online at [ohre.unc.edu/sops.php](http://ohre.unc.edu/sops.php) starting with IRB SOP 24.0. “IRB Evaluation Criteria.”

### RISK

Minimal risk (for human subjects other than prisoners) 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. [21CFR50.3(k), 21CFR56.102(i), 45CFR46102(i)]

Risk should be considered in terms of both severity and probability, and should not be understood to apply to only physical risk, though such risks are important to consider. In reviewing a study, the IRB evaluates emotional and psychological risks, potential insurability risks, as well as risks to professional or community standing. For example, in conducting a drug use survey, respondents could face severe penalties in the workplace or in their community though the survey itself does not represent a physical or psychological risk.

Risks to subjects must be minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

Risks to subjects must be reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.

### BENEFIT

In assessing the potential benefits of a study, researchers should consider the direct benefit to potential participants in the study (as may be the case in a study providing access to a valuable intervention) as well as the long term societal benefits that the study may make possible through generalizable knowledge.

### SELECTION OF SUBJECTS

In accordance with Belmont principles, both the burdens and benefits of research should be distributed equitably. Equitable distribution of research burdens and benefits is an important factor in the selection of subject populations for a study.

### REVIEW AND DOCUMENTATION OF INFORMED CONSENT

Informed consent practices must conform to those described in Section 10 below. The informed consent process is one of the most important investigator responsibilities in human subjects research.

### SAFETY MONITORING

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

## PRIVACY OF SUBJECTS AND CONFIDENTIALITY OF DATA

There should be adequate administrative, procedural and technical provisions to protect the privacy of subjects and to maintain the confidentiality of data. See also HIPAA section below.

## ADDITIONAL SAFEGUARDS FOR VULNERABLE SUBJECTS

When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, decisionally impaired persons, or economically or educationally disadvantaged persons, or to have other vulnerability, such as pregnant women, additional safeguards must be included in the study to protect the rights and welfare of these subjects.

## RECRUITMENT AND PAYMENT OF SUBJECTS

Researchers must use appropriate methods for identifying and recruiting potential research subjects and compensating participating subjects.

## FUNDING PROPOSAL OR CONTRACTUAL STATEMENT OF WORK

Funding proposals and contractual statements of work must be congruent with the protocol approved by the IRB.

## REQUIRED EDUCATION AND CERTIFICATION OF INVESTIGATORS ON HUMAN RESEARCH ETHICS

Anyone who will come in contact with human subjects or human subject data (faculty, staff or students) must receive the training described in the University's "[Policy on Education and Certification of Investigators Involved in Human Subjects Research](#)" regardless of source of funding of research.

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## 10. MAJOR INVESTIGATOR RESPONSIBILITIES AFTER IRB INITIAL APPROVAL

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### INFORMED CONSENT – A PROCESS

**Informed consent is a process rather than merely a document.** Any subject invited to participate in a research study should be given a description of the study that is clear and complete enough for the individual to judge whether she or he wants to participate. The informed consent process should be designed to provide the potential subjects with readily understandable information in an amount and timing appropriate to the level of risk in participating.

The subject's consent must follow and not precede receipt of this information unless the IRB approves a different procedure (as in some behavioral research that would be compromised by full disclosure in advance). Consent must be obtained from each subject who is legally, mentally, and physically able to provide it unless waived by the IRB. Consent should be in writing unless the IRB finds that written documentation of informed consent may be waived. Consent forms and informational letters should be written in simple language so as to be easily understood by persons with no technical background in the field.

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.

The standard consent process and documentation is that all subjects will sign a document containing all the elements of informed consent, as specified in the federal regulations. The OHRE provides an informed consent template (see below). Some or all of the elements of consent, including signatures, may be waived under certain circumstances. Unless waived by the IRB, participants must sign and date the consent form prior to participation in the study. At the time of review, the IRB will determine whether or not the person obtaining consent may be required to sign and date the form. The signed consent form should be retained in the investigator's files and a copy of the signed consent form should be provided to the person giving consent.

### UNC-CHAPEL HILL CONSENT FORM TEMPLATES

The [Consent Form templates](#) should be used for all written consent form documents. This consent template contains all of the basic elements described above. For clarity and to assure timely processing by the IRB, the consent form should follow the guidelines described below.

The consent form and study fact sheet must be written at a level understandable to all potential participants and it must contain all information that would reasonably influence the subject's willingness to participate. In order to facilitate this requirement, the IRB will provide templates which reflect appropriate language for various subject populations. The consent form should be written in second person with "you" or "your child" consistently used to refer to the subject in all statements.

In most cases, the title of the project as listed on the consent form should be the same as the title listed on the application form, though the IRB may suggest or require modifications in the title under certain circumstances (for example, in case the title would alert subjects to deception in the study or when the title may be too explicit regarding subject criteria as in a study of dysfunctional parents).

The date on which the consent form was prepared should be indicated on the form so that revised forms can be easily distinguished from prior drafts.

#### WAIVER OF INFORMED CONSENT

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

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

The IRB application form includes a section for requesting waiver of the informed consent requirement. The IRB application form also addresses whether HIPAA is applicable to the study and includes a section for requesting waiver of the HIPAA requirement for authorization, if applicable.

#### REPORTING ADVERSE EVENTS AND UNEXPECTED PROBLEMS IN HUMAN SUBJECTS RESEARCH

##### DEFINITIONS

An adverse event is an undesirable and unintended, though not necessarily unanticipated, injury or physical or emotional consequence to a human subject.

Serious Adverse Events (SAEs) are those that are fatal or life threatening; that result in significant or persistent disability; that require or prolong hospitalization; that result in a congenital anomaly/birth defect; or that, in the opinion of the investigators, represent other significant hazards or potentially serious harm to research subjects or others.

Unexpected or unanticipated refers to adverse events or other problems in the research, the specificity or severity of which is not consistent with the information already provided to the IRB, including the investigator's brochure, research protocol or consent form.

Unanticipated Problems (UPs) may or may not include specific events experienced by individual subjects, but are developments within the research activity that suggest a potential for increased risks to subjects or others.

##### INVESTIGATOR RESPONSIBILITIES REGARDING SERIOUS ADVERSE EVENTS (SAE) OR UNANTICIPATED PROBLEMS

In case of a Serious Adverse Event or an Unanticipated Problem, the PI is required to submit a written report (see below) to the IRB, with the time frame for the report depending on the type of event being reported. The PI's report should contain enough information for the IRB to judge whether or not the event raises new questions about risks to participants or the research design.

In case of an adverse event that is **both serious and unanticipated** which occurs at a site for which a UNC-Chapel Hill IRB has direct oversight responsibility, the PI must notify the IRB within 24 hours (or by the next working day).

In case of an adverse event that is **serious but not unanticipated**, the PI must notify the IRB within 5 working days.

In case of an adverse event that is **not serious, but is unanticipated**, the PI must notify the IRB within 10 working days.

In case of an **UP involving risks to subjects or others but not meeting the definition of an adverse event**, the PI must notify the IRB within 10 working days.

#### ADVERSE EVENT WRITTEN REPORT

In case of any adverse event, the PI should file an Adverse Event Written Report with the IRB. Typically, this report serves as the notification described above. However, in case of an SAE, the investigator will most likely notify the IRB immediately and file the report as soon as possible thereafter.

The Adverse Event Written Report must contain the following information:

- IRB study number
- Title of protocol
- Name of principal investigator and relevant department, division or center.
- Subject identifier (study number/reference of subject)
- Date and site of event
- Description of event (nature of injury or other adverse occurrence, assessment of severity, and assessment of relationship to study)
- Handling/response to the event
- Any proposed changes in protocol or consent form due to event
- To whom else the event has been reported
- Signature of principal investigator

#### **IRB APPROVAL REQUIRED FOR ALL MODIFICATIONS AND AMENDMENTS TO PREVIOUSLY APPROVED PROTOCOLS**

A modification is a change in an approved research protocol. IRB review and approval is required before investigators can modify research protocols, except when necessary to eliminate apparent immediate hazards to the subjects. Any proposed change to a previously approved project must be submitted to the IRB as an amendment to that project and may be reviewed by the expedited IRB review procedure or by the convened IRB, depending on the IRB chair's assessment of associated risk. Minor changes in previously approved research may be approved by expedited IRB review. Minor changes are those that do not significantly alter the risks/benefits balance or other study elements. OHRE has a form for requesting approval of a modification on its [forms web page](#).

#### CONTINUING REVIEW

The IRB will conduct continuing review of UNC Chapel Hill human subjects research studies covered by this policy at intervals appropriate to the degree of risk, but not less than once per year. Investigators should submit renewal forms at least 30 days before the end of the approval period for their study. A lapsed study is one for which the approval period has expired prior to the renewal of

approval by the IRB. If a PI wishes to continue research on a lapsed study, he or she must wait for approval before continuing any research related procedures.

When a research project is due for continuing review, a written reminder is sent on behalf of the IRB to the PI (and, when applicable and if possible, the TI) approximately 60-90 days before the date of continuing review. Another reminder is sent approximately 30-60 days prior to the review date. If an application for renewal is not received from the PI by the expiration date, then the IRB will send an expiration notice to the PI.

The OHRE provides a [renewal form](#) on its web site for the submission of continuation materials. The application for continuing review will include a progress report in which the PI describes the number of subjects enrolled, any problems that occurred during the prior approval period, any changes being requested as a part of the current renewal.

Following IRB review of the application for continuing review, investigators are notified in writing of the decision of the IRB and any changes required. Final approval is not granted until all required changes have been made and submitted for review and approval.

## STUDY COMPLETION

Research studies can be deemed completed for a number of reasons, each requiring a different degree of IRB involvement. Most often, the investigator or sponsor will close the study and the IRBs role is passive, receiving study completion documents and archiving the records for the study. In some cases, the IRB must perform in a supervisory or disciplinary fashion and require that a study be ended.

### *Voluntary completion by investigators*

By submitting a [notice of completion](#), the researcher confirms that the study is finished and that researchers have no further interaction with subjects or their data. Once the IRB receives and accepts the study completion form, the researcher is no longer required to submit for continuing review for renewal. If the investigator wishes to enroll new subjects for the study, or otherwise engage human subjects in research, he/she must reactivate the protocol with the IRB. Therefore, an investigator should only close a study when he/she is no longer enrolling new subjects, using research interventions on existing subjects, collecting data (including follow-up data), or performing any other tasks that were identified as part of the approved study. A study will not invariably be considered completed when it is closed to accrual, as research-related procedures may still be continuing. The IRB, in consultation with the PI, may consider closing a study when active data analysis and publication pursuant to the approved study has ceased, even if the investigator retains records that may identify individual subjects. Additional research projects using data acquired in the approved study may constitute new human subjects research studies subject to separate IRB review.

### *Expiration of approval period*

Once the approval period for a given study has expired prior to the renewal of approval by the IRB, it is considered a lapsed study and all research-related procedures must halt, except where doing so would jeopardize the welfare of the human subjects. If the PI fails to submit the materials for continuing review within one month following the expiration date, then the lapsed study will be classified as inactive. If the PI submits the materials for continuing review within one month following the expiration date, the IRB will conduct continuing review and reactivate the protocol. This reactivation establishes a new approval period that is not retroactive to the prior date of expiration. If the PI desires to continue a study that has lapsed for more than one month, then the

PI must submit a new application for re-review by the IRB, and must wait for IRB approval before resuming research under the protocol.

*Termination of a study by the IRB*

In cases of Serious Adverse Events (SAEs) or Unanticipated Problems (UPs) (see 7.b. above), cases of researcher noncompliance, or in cases of protocol violations, the IRB may decide to suspend a study to ensure subject safety. Upon investigation of the problem prompting suspension of the study, the convened IRB may decide that a study should be terminated. Following the vote of the IRB to terminate a study and the evaluation of any appeals made by the PI, the study will be classified as closed. Though the chair may suspend a study, pending IRB review, only the convened IRB may vote to terminate a study.

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## 11. ADDITIONAL GUIDANCE ON SPECIFIC TOPICS

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Additional guidance for the topics listed below can be found in the [Standard Operating Procedures](#) for the IRBs of the [Office of Human Research Ethics](#).

### RECRUITMENT

- Advertisements
- Direct Solicitation
- Requests from outside researchers to solicit on the UNC-Chapel Hill campus

### RECRUITMENT INCENTIVES

- Payments to research study participants
- Finders fees, enrollment bonuses, etc.
- Lotteries, raffles and door prizes

### INVESTIGATOR CONFLICT OF INTEREST

- Investigator Conflict of Interest: Internal Disclosure Requirements
- Investigator Conflict of Interest: University Review Coordination with IRB
- Summary of University Policy on Conflict of Interest in Human Subjects Research
- Compensation from Sponsors

### INFORMED CONSENT

- Basic Elements of Informed Consent
- Additional Elements of Informed Consent
- Exceptions to informed consent requirements
- Other exceptions to informed consent requirements 45 CFR 46.116(d)
- Other information concerning informed consent
- Short form consent procedures
- Waiver of written consent
- UNC-Chapel Hill Consent Form templates
- Assent by children
- Surrogate consent for subjects who are decisionally impaired
- Obtaining consent from non-English speaking subjects
- Translation and informed consent
- Consent for use of stored samples and genetic testing
- Consent for inclusion in research registry
- Verifying subject consent
- Stamped copies of consent forms
- Informed consent forms in health care records
- Record retention of informed consent forms

## HIPAA AND IRB REVIEW

- HIPAA Authorization and Informed Consent
- Procedure for Signing an Authorization
- HIPAA Waiver of Authorization
- Limited Waiver of Authorization solely for the purpose of prescreening, contacting and/or recruiting potential research participants

## SPECIAL TOPICS: RESEARCH DESIGN AND CONTEXT

- Research in educational settings
- Trainee-led projects
- Class projects involving human subjects research
- Pilot studies
- Oral histories as a type of humanities or social science research
- Qualitative research
- Survey research
- Investigational New Drug and Investigational Device Exemption studies
- Research involving radiation
- Multi-center studies for which UNC-Chapel Hill is the coordinating center
- Research using existing data and materials
- Review involving data from voice, video, digital or image recordings
- Research involving deception or withholding of information
- Research involving potentially addictive substances
- Genetic information in research
- Gene manipulation in human subjects research
- Human embryonic stem cell research
- Human fetal tissue transplantation research
- Family history research
- Internet research
- Self-experimentation

## SPECIAL TOPICS: INTERNATIONAL RESEARCH

- Human Subjects protection administration issues
- Risk
- Justice/Benefit
- Understanding the protocol and consent process

## SPECIAL TOPICS: RESEARCH SUBJECT GROUPS

- Elements to consider in research involving vulnerable subjects
- Pregnant women and neonates
- Prisoners
- Children
- Decisionally impaired subjects
- Research involving other potentially vulnerable adult subjects
- Research involving decedents
- Third party research subjects
- Employees, students or trainees as research subjects

## RESEARCH INVOLVING PREGNANT WOMEN AND NEONATES

- Conditions required for pregnant women or neonates to be involved in research
- Conditions required for neonates of uncertain viability and nonviable neonates to be involved in research
- Neonates of uncertain viability
- Nonviable neonates
- Viable neonates

## RESEARCH INVOLVING PRISONERS

- Definition of research addressed in this section
- Issues to be addressed in reviewing research involving prisoners
- Types of research conducted or supported that may involve prisoners as subjects:
- Certification of prisoner research

## RESEARCH INVOLVING CHILDREN

- Research in health care settings
- Research in school settings

## CATEGORIES OF RESEARCH INVOLVING CHILDREN THAT MAY BE APPROVED BY IRBS