

standard operating

*Policies &
Procedures*

HOMEWOOD
HIRB
Institutional Review Board
JOHNS HOPKINS
UNIVERSITY

Note: The Homewood Institutional Review Board (HIRB) oversees research in the following divisions of the Johns Hopkins University: the Applied Physics Laboratory (for behavioral and social sciences research), Carey School of Business, Krieger School of Arts and Sciences, Peabody Institute, School of Advanced International Studies, and School of Education, Whiting School of Engineering. For the sake of simplicity, these divisions are referred to as the Homewood Schools or the Homewood Divisions in HIRB documents and communications.

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Table of Contents

Section One: Ethical Principles & IRB Oversight.....	1
Introduction.....	1
Section Objective.....	1
Relevant Definitions.....	1
1.1 Ethical Principles.....	2
<i>The Belmont Report</i>	2
<i>The Nuremberg Code and The Declaration of Helsinki</i>	3
1.2 Federal Regulations.....	3
1.3 Federalwide Assurance (FWA).....	3
1.4 IRB Agreements Covering Investigators Outside the Homewood Schools.....	4
<i>JHM Reciprocity Agreements</i>	4
<i>Collaborating Investigators with IRBs</i>	5
<i>Collaborating Individual Investigators Without IRBs</i>	5
<i>Statistical and Coordinating Centers</i>	7
<i>Homewood Personnel Assisting Non-JHU PIs</i>	8
Section Two: HIRB Authority & Operation	1
Introduction.....	1
Section Objective.....	1
Relevant Definitions.....	1
2.1 HIRB Authority.....	2
2.2 Institutional Official (IO).....	3
2.3 HIRB Personnel.....	4
<i>HIRB Members</i>	4
<i>HIRB Chair</i>	4
<i>HIRB Director</i>	5
<i>HIRB Office Staff</i>	6
2.4 HIRB Consultants.....	7
2.5 HIRB Meetings.....	7
2.6 HIRB Member Conflicts of Interest.....	8
2.7 HIRB Review.....	8
2.8 HIRB Reports.....	8
2.9 HIRB Monitoring Activities.....	9

<i>Routine Audits</i>	Error! Bookmark not defined.
<i>Random Audits</i>	9
<i>For-Cause Audits</i>	9
<i>HIRB Actions Following Audits</i>	9
Section Three: Investigator Responsibilities	11
Introduction	11
Section Objective	11
Relevant Definitions	11
3.1 Investigator Qualifications	12
3.2 General Responsibilities	12
<i>Conduct of the Research</i>	12
<i>Record Keeping and Reporting</i>	13
<i>Monitoring and Oversight</i>	14
<i>Communication</i>	14
<i>Education and Training</i>	14
3.3 Investigator Conflicts of Interest	14
3.4 Data Safety and Monitoring	15
<i>Data Safety and Monitoring Plan Elements</i>	16
3.5 Certificates of Confidentiality	17
<i>When a Certificate of Confidentiality Is Appropriate</i>	17
<i>Protections Afforded by a Certificate</i>	18
<i>Mandatory Reporting Requirements</i>	18
<i>Requirements for Informed Consent</i>	19
<i>International Studies</i>	19
<i>Applying for a Certificate of Confidentiality</i>	19
3.6 Reportable Diseases and Conditions	19
<i>Reportable Diseases</i>	19
<i>Reportable Abuse and Harm</i>	20
<i>Investigator Responsibilities</i>	20
Section Four: Education & Training	1
Introduction	1
Section Objective	1
Relevant Definitions	1
4.1 HIRB Member Training	2
4.2 HIRB Staff Training	2
4.3 Investigator Training Requirements	2
4.4 Outreach Activities	3
<i>HIRB Newsletter</i>	3

<i>Brown Bag Sessions</i>	3
<i>Educational Materials and Guidelines</i>	3
<i>Consultation with HIRB Office Staff</i>	3
<i>Local, Regional, and National Meetings and Courses</i>	3
Section Five: Review Procedures: Applications for New Research	4
Introduction	4
Section Objective	4
Relevant Definitions	4
5.1 What Constitutes Human Participant Research and Is Subject to HIRB Review	5
5.2 Institutions Engaged in Research	7
<i>Engaged in Research Examples</i>	8
<i>Not Engaged in Research Examples</i>	9
5.3 When Homewood Personnel Assist a Non-JHU PI	11
5.4 HIRB Review Levels	12
5.5 Application Procedures for New Studies	12
<i>Supporting Documents and Checklists</i>	Error! Bookmark not defined.
<i>Common Application Mistakes</i>	13
<i>When and Where to Submit Applications for New Studies</i>	13
5.6 HIRB Review — Exempt	14
<i>Exempt Categories</i>	14
5.7 HIRB Review — Expedited	16
5.8 HIRB Review — Full Board	18
5.9 Criteria for HIRB Exemption and Approval of New Studies	19
<i>Exemption</i>	Error! Bookmark not defined.
<i>Approval</i>	Error! Bookmark not defined.
5.10 HIRB Determinations and Motions	20
<i>Exempt Review</i>	20
<i>Expedited and Full Board Review</i>	20
5.11 Application Revisions	21
<i>Guidance on Submission of Revisions</i>	Error! Bookmark not defined.
5.12 Appeal of HIRB Decisions	22
Section Six: Review Procedures: Ongoing Research	1
Introduction	1
Section Objective	1
Relevant Definitions	1
6.1 Amendments and Changes to Approved Studies	2
<i>Amendments and Changes that Do Not Alter the Risk/Benefit Ratio</i>	2
<i>Amendments and Changes that May Alter the Risk/Benefit Ratio</i>	3

	<i>Guidance on Submission of Proposed Amendments and Changes</i>	3
	<i>HIRB Review of Requests for Amendments and Changes</i>	4
6.2	Continuing Review	4
	<i>Deadline for Continuing Review</i>	5
	<i>General Guidelines for Progress Reports</i> Error! Bookmark not defined.	
	<i>Specific Guidelines Based on Project Status</i>	5
	<i>HIRB Review of Applications for Continuing Review</i>	6
6.3	Closing Studies	7
	<i>Retaining Records After Closure</i>	7
Section Seven:	Requirements for Specific Research Activities	1
	Introduction	1
	Section Objective	1
	Relevant Definitions	1
7.1	Class Projects	2
	<i>Policies and Procedures</i>	2
	<i>Education Requirements</i>	3
7.2	Individual Student Research Projects	3
	<i>Education Requirements</i>	4
	<i>Applying for HIRB Review</i>	4
	<i>Faculty Supervisor Responsibilities</i>	4
	<i>Student Leave of Absence</i>	
7.3	Research at International Sites	5
	<i>Federal Regulations</i>	6
	<i>Local Approval</i>	6
	<i>Informed Consent</i>	7
	<i>Additional Considerations</i>	7
7.4	Research in Educational Settings	8
7.5	Research via the Internet	9
	<i>Recruitment Process</i>	9
	<i>Risks and Benefits</i>	10
	<i>Informed Consent</i>	10
	<i>Confidentiality</i>	11
	<i>Web Site Content</i>	11
	<i>HIRB Review</i>	11
7.6	Research with Human Biological Materials	12
7.7	Program Evaluation	12
7.8	Oral History Studies	13
7.9	Self-Experimentation	14
7.10	Research Supported by Grants or Contracts	14

7.11	Pilot Activities	14
7.12	Multi-Site Studies.....	15
	<i>Non-JHU Sites</i>	15
	<i>Statistical and Coordinating Centers</i>	15
7.13	Studies Transferred to JHU	16
7.14	Research Without a Definite Plan to Involve Human Participants	16
Section Eight:	Informed Consent Process	1
	Introduction.....	1
	Section Objective.....	1
	Relevant Definitions.....	1
8.1	Federal Regulations	2
8.2	Required Elements of Informed Consent	2
8.3	Waivers and Alteration of Informed Consent.....	3
	<i>Waivers for FDA-Regulated Studies</i>	4
	<i>Applying for Waivers and Alterations</i>	5
8.4	Emergency Waivers	5
8.5	Deception of Participants	6
8.6	Tests of Understanding	6
	<i>Oral Tests</i>	7
	<i>Written Tests</i>	7
	<i>Feedback and Failure to Pass Tests</i>	8
8.7	Participants Unable to Consent.....	8
8.8	Child Assent/Parental Permission	8
	<i>Child Consent Without Parental Permission</i>	9
8.9	Decisionally-Impaired Adults	10
	<i>Selecting Participants and Obtaining their Consent</i>	10
8.10	Consent in Languages Other Than English.....	12
8.11	Consent via Phone	12
8.12	Secondary Research Participants	13
Section Nine:	Consent Documents	1
	Introduction.....	1
	Section Objective.....	1
	Relevant Definitions.....	1
9.1	Regular and Short Consent Forms.....	2
9.2	Guidelines for Consent Forms.....	2
	<i>Title of Research Project</i>	2
	<i>Purpose of Research Study</i>	3

<i>Procedures</i>	3
<i>Risks/Discomforts</i>	4
<i>Benefits</i>	4
<i>Voluntary Participation and Right to Withdraw</i>	5
<i>Circumstances that Could Lead Us to End Your Participation</i>	5
<i>Alternatives to Participation</i>	5
<i>Confidentiality</i>	6
<i>Costs</i>	6
<i>Compensation</i>	7
<i>If You Have Questions or Concerns</i>	7
<i>If You Are Harmed by Participating in the Study</i>	8
<i>Sharing of New Findings</i>	8
9.3 Tips for Writing Consent Forms	8
<i>Format, Style, and Reading Level</i>	8
<i>Consent Information Investigators Often Overlook</i>	9
<i>Improving Understanding</i>	10
9.4 Exculpatory Language.....	10
9.5 Review and Approval of Consent Forms.....	11
Section Ten: Participant Recruitment & Compensation	1
Introduction	1
Section Objective.....	1
Relevant Definitions.....	1
10.1 Recruitment Materials.....	1
10.2 Recruitment of Minorities and Women.....	3
10.3 Recruitment of JHU Students	4
<i>Recruitment</i>	4
<i>Participation Incentives</i>	5
<i>Minimal Risk Research</i>	5
<i>Greater than Minimal Risk Research</i>	5
<i>Confidentiality</i>	6
<i>HIRB Approval</i>	6
10.4 Recruitment and Enrollment of JHU Employees	6
<i>Recruitment</i>	6
<i>Minimal Risk Research</i>	6
<i>Greater than Minimal Risk Research</i>	6
<i>Confidentiality</i>	7
10.5 Payment to Participants.....	7
10.6 Compensation for Injury.....	8
10.7 Right of Participants to Withdraw.....	9

Section Eleven: Vulnerable Populations	1
Introduction	1
Section Objective	1
Relevant Definitions	1
11.1 Children	2
<i>Justifications for Excluding Children from Research</i>	2
<i>Allowable Categories of Research Involving Children</i>	3
<i>Child Assent/Parental Permission</i>	4
<i>Child Consent Without Parental Permission</i>	5
<i>Research Conducted in Public Schools</i>	5
<i>Wards of the State</i>	6
11.2 Pregnant Women, Fetuses, and Neonates	6
<i>General Guidelines</i>	6
<i>Research Involving Women Who Are, or May Become, Pregnant</i>	7
<i>Pregnancy Testing</i>	7
<i>Allowable Research Involving Pregnant Women or Fetuses Prior to Delivery</i>	8
<i>Allowable Research Involving Neonates</i>	9
<i>Allowable Research with Human Fetal Tissue, Placenta, or Post Delivery Fetal Material</i>	9
<i>Allowable Research Not Otherwise Approvable</i>	10
11.3 Prisoners	10
<i>Allowable Categories of Research Involving Prisoners</i>	10
<i>Additional Requirements for Research that Involves Prisoners</i>	11
<i>Research Involving Participants Who Become Prisoners After Enrollment</i>	12
<i>Required Review by OHRP</i>	12
11.4 Decisionally-Impaired Participants	12
<i>Selecting Participants and Obtaining their Consent</i>	13
11.5 Other Vulnerable Populations	14
Section Twelve: Adverse Events & Unanticipated Problems	1
Introduction	1
Section Objective	1
Relevant Definitions	1
12.1 Adverse Events	3
<i>Monitoring Adverse Events in Studies with Greater than Minimal Risk</i>	3
<i>Data Safety and Monitoring Plan</i>	4
<i>Who May Serve as a DSM or Member of a DSMB or SMC</i>	4
<i>Reporting Adverse Events</i>	5
12.2 Unanticipated Problems	6
<i>What Needs to Be Reported</i>	6
<i>Who Should Report Unanticipated Problems</i>	6

<i>When and How to Report Unanticipated Problems</i>	7
<i>Reporting for Multi-Site Studies and Coordinating Centers</i>	7
12.3 HIRB Responses to Reports of Unanticipated Problems	7
12.4 Reporting Unanticipated Problems to JHU Officials and Outside Agencies	8
Section Thirteen: Noncompliance	1
Introduction.....	1
Section Objective.....	1
Relevant Definitions.....	1
13.1 Reports and Allegations of Noncompliance.....	2
13.2 Minor Noncompliance	2
<i>HIRB Response to Reports of Minor Noncompliance</i>	3
<i>HIRB Response to Allegations of Minor Noncompliance</i>	3
13.3 Serious, Continuing, and Intentional Noncompliance	3
<i>HIRB Response to Reports of Serious and Continuing Noncompliance</i>	4
<i>HIRB Response to Allegations of Serious and Continuing Noncompliance</i>	5
<i>HIRB Response to Possible Intentional Noncompliance</i>	5
13.4 Suspension and Termination of Studies (Withdrawal of HIRB Approval)	5
13.5 Reporting Noncompliance to JHU Officials, OHRP, and Others	6
13.6 Complaints Regarding Human Participant Research	7
Section Fourteen: Records & Documentation	1
Introduction.....	1
Section Objective.....	1
Relevant Definitions.....	1
14.1 HIRB Office Records	1
14.2 HIRB Meeting Agendas	2
14.3 HIRB Minutes.....	3
<i>General Requirements</i>	4
<i>Specific Findings</i>	4
<i>Participation via Phone</i>	5
<i>Distribution and Approval of Minutes</i>	5
14.4 Development and Approval of HIRB Policies and Procedures	6
Appendix A: Flow Charts	1
Chart 1. Is It Human Participant Research, as Defined by Federal Regulations?	2
Chart 2. Is the Study Eligible for Exemption?	3
Chart 3. Does Exempt Category 1 (Educational Settings) Apply?	4
Chart 4. Do Exempt Cats. 2 & 3 (Ed. Tests, Surveys, Interviews, Public Obs.) Apply?	5

Chart 5. Does Exempt Category 4 (Existing Data and Specimens) Apply?.....	6
Chart 6. Does Exempt Category 5 (Public Benefit and Service Programs) Apply?	7
Chart 7. Does Exempt Category 6 (Food Taste and Acceptance Studies) Apply?.....	8
Chart 8. Is the Study Eligible for Expedited Review?	9
Chart 9. Can Informed Consent Requirements Be Waived or Altered?	10
Chart 10. Can Documentation of Informed Consent Be Waived?.....	11
Chart 11. Are Secondary Research Participants Involved?	12
Chart 12. Is Informed Consent Needed from Secondary Research Participants?.....	13

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Section One: Ethical Principles & IRB Oversight
Date of Revision: 11/17/14

Introduction

Johns Hopkins University (JHU) is committed to protecting the rights and welfare of individuals participating in research. All human participant research conducted under the auspices of JHU is evaluated by an institutional review board (IRB) to ensure that the rights and welfare of participants are fully protected in keeping with accepted ethical principles and Federal regulations governing human participant research, as well as other applicable Federal, international, state, and local laws and regulations. The Homewood Institutional Review Board (HIRB) oversees human participant research conducted by personnel in the Homewood Divisions, which consist of the Applied Physics Laboratory, Carey Business School, Krieger School of Arts and Sciences, Peabody Institute, School of Advanced International Studies, School of Education, and Whiting School of Engineering.

Section Objective

The purpose of this section is to introduce the ethical principles and Federal regulations that govern oversight of human participant research by IRBs. The Homewood Schools' Federalwide Assurance (FWA) is described, and agreements and procedures that affect collaborating investigators outside the Homewood Schools are detailed.

Relevant Definitions

AUTHORIZATION AGREEMENT A joint agreement, approved by OHRP, in which multiple institutions agree to participate in a research project while relying on the review of one primary IRB's review and approval in order to avoid duplication of effort.

COMMON RULE Another name for 45 CFR 46, Subpart A, the Federal regulations governing the protection of human research participants. Eighteen Federal departments and agencies have adopted the Common Rule and require institutions, such as JHU, that receive their support to comply with these regulations.

FEDERALWIDE ASSURANCE (FWA) A written, binding commitment submitted to OHRP by an institution engaged in human participant research in which the institution promises to comply with applicable Federal regulations governing such research and specifies the procedures it will follow to ensure compliance [45 CFR 46.103]. The Johns Hopkins University Homewood Schools' Federalwide Assurance is No. 00005834.

HRPP (HUMAN RESEARCH PROTECTIONS PROGRAM) The array of protections that are in place throughout the Homewood Divisions to ensure the rights and safety of human participants in research associated with the divisions.

HIRB The Homewood Institutional Review Board, which is the IRB that reviews research associated with the JHU Homewood Divisions.

HOMEWOOD DIVISIONS The Johns Hopkins University Applied Physics Laboratory, Carey Business School, Krieger School of Arts and Sciences, Peabody Institute, School of Advanced International Studies, School of Education, and Whiting School of Engineering.

IRB OF RECORD An IRB is considered the IRB of Record when it assumes IRB responsibilities for another organization.

OHRP (OFFICE FOR HUMAN RESEARCH PROTECTIONS) An administrative office within the Department of Health and Human Services (DHHS). OHRP implements Federal regulations for the protection of human research participants [45 CFR 46] and provides guidance on ethical issues in biomedical and behavioral research.

1.1 Ethical Principles

The rights and safety of individuals participating in research are assured through adherence to widely accepted ethical principles that were established for biomedical experiments and extended to behavioral research.

The Belmont Report

All human participant research activities conducted by investigators affiliated with the Homewood Divisions should be guided by the ethical principles of respect for persons, beneficence, and justice, each of which is described in *The Belmont Report* (<http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html>) as excerpted below.

- **Respect:** “Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection.”
- **Beneficence:** “Two general rules have been formulated as complementary expressions of beneficent actions in this sense: (1) do not harm and (2) maximize possible benefits and minimize possible harms.”
- **Justice:** “Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of ‘fairness in distribution’ or ‘what is deserved.’” More specifically, “the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.”

All Homewood faculty, staff, and students, as well as collaborating investigators, who are involved in human participant research are expected to be knowledgeable of the principles outlined in *The Belmont Report* and to apply them in the conduct of human participant research to ensure participants’

rights and protection from harm. Homewood Institutional Review Board (HIRB) members and staff also are required to be familiar with these principles and apply them to the review and oversight of human participant research.

The Nuremberg Code and The Declaration of Helsinki

The Nuremberg Code and *The Declaration of Helsinki* are two other important documents that have established principles for the ethical treatment of human participants in biomedical and behavioral research. *The Nuremberg Code* of 1947 is a landmark document that has informed ethics guidelines worldwide. Developed during the Nuremberg Doctors' Trial, it laid out criteria for ethical medical research, in stark contrast to the horrific medical experiments conducted by Nazi doctors. Among the ten conditions specified for ethical medical experiments are voluntary informed consent and the weighing of risks against expected benefits. *The Declaration of Helsinki* was drawn up by the World Medical Association (WMA) in 1964, also in response to the medical atrocities committed during WWII, and is the WMA's most well-known policy statement. *The Declaration of Helsinki* specifies ethical principles for doctors involved in medical research with human participants and has been extended to behavioral research by nonphysicians. Amended several times since 1964, the 2004 version is the most recent and official document.

1.2 Federal Regulations

HIRB reviews all human participant research in accordance with the Federal Policy for the Protection of Human Subjects (also known as the Common Rule) and additional subparts contained in Title 45 Code of Federal Regulations Part 46 (45 CFR 46, subparts A, B, C, & D). In addition, HIRB ensures that all research regulated by the Food and Drug Administration (FDA) complies with requirements set forth in 21 CFR 50, 21 CFR 56, 21 CFR 312, and 21 CFR 812 and with any regulations or policies of other Federal departments and agencies, such as the National Institutes of Health and the Department of Education, supporting the research under review. HIRB also determines whether research is exempt from the Common Rule, as allowed by those regulations. The Common Rule does not affect applicable state, local, or foreign laws or regulations that provide additional protections for human participants. Therefore, HIRB ensures that all human participant research complies with applicable state and local laws. When research is conducted in a foreign country, HIRB abides by applicable foreign laws that provide additional protections to individuals participating in research.

Furthermore, the Research Projects Administration Office and the JHU Office of General Counsel assist in ensuring that human participant research activities under HIRB's jurisdiction are compliant with Federal, state, and local laws and regulations.

1.3 Federalwide Assurance (FWA)

The JHU Homewood Divisions have committed to a Federalwide Assurance (FWA) with the Office for Human Research Protections (OHRP). The Homewood FWA is a formal agreement by the Homewood Divisions to protect the rights and safety of all individuals who participate in research. The Homewood Schools' FWA assures that all nonexempt human participant research conducted by Homewood faculty, staff, and students will be reviewed and approved by an IRB and subject to continuing review by an IRB, in a manner consistent with the principles set forth in *The Belmont Report* and Federal regulations (45 CFR 46 and subparts A, B, C, & D), regardless of the funding source for the research, lack of funding, or where the research is performed. The JHU Homewood

Schools' Federalwide Assurance (No. FWA00005834) covers HIRB. The FWA number should be cited on all relevant grant and contract applications involving human participant research.

Under the FWA, the Homewood Divisions are responsible for:

1. Designating one or more IRBs to provide scientific and ethical review and approval of all nonexempt research covered by the FWA.
2. Providing sufficient resources, space, and staff to support HIRB's review, monitoring, and record-keeping responsibilities.
3. Providing training and educational opportunities for HIRB members and investigators.
4. Developing policies and procedures for effective and efficient administration of the Homewood Human Research Protection Program (HRPP).
5. Ensuring that assurances are in place and that certification of HIRB review is submitted to the appropriate authorities for all of the Homewood Divisions' Federally-sponsored research, including research done at collaborating performance sites, as appropriate.
6. Implementing appropriate oversight mechanisms to ensure compliance with regulations and effective administration of the Homewood HRPP.

1.4 IRB Agreements Covering Investigators Outside the Homewood Schools

Investigators who conduct human participant research with collaborators outside the JHU Homewood Schools must adhere to special provisions concerning IRB review of their research. There are five typical scenarios, not mutually exclusive, in which Homewood personnel collaborate in the conduct of research with investigators outside the Homewood Schools.

1. A PI or co-investigator is a member of Johns Hopkins School of Medicine (JHM). See Reciprocity Agreements below.
2. A Homewood PI, investigator, or consultant collaborates with one or more investigators from non-JHU institutions with their own IRBs. This is common in multi-site studies. See Collaborating Investigators with IRBs below.
3. Homewood personnel collaborate with one or more individuals outside the Homewood Schools who are not connected to an institution that has its own IRB. See Collaborating Individual Investigators without IRBs below.
4. A statistical or coordinating center for a multi-site study is located in the JHU Homewood Schools or headed elsewhere by a Homewood PI. See Statistical and Coordinating Centers in this section.
5. Homewood personnel, not co-investigators, engage in research by assisting a non-JHU PI. For instance, Homewood personnel help an outside investigator enroll students on the Homewood campus in the non-JHU PI's study. (See Section 5.1 through 5.3 for more information on engagement in research.)

Reciprocity Agreements

HIRB has entered into a reciprocity agreement with the Johns Hopkins Medicine (JHM) for review of human participant research that is jointly performed by investigators from these divisions. Under

these agreements, the IRB of the institution in which the PI has his or her primary appointment usually will serve as the single IRB of Record for the project. Generally, a Homewood PI should submit his or her application to HIRB, regardless of the funding source or the participant population. A Homewood investigator who is involved in research with a PI whose primary appointment is in JHM does not need to submit a separate application to HIRB. In such cases, the appropriate JHM IRB will serve as the single IRB of Record for the study. The purpose of this policy is to eliminate duplicative protocol review by multiple IRBs within JHU.

There are several exceptions to this policy. One exception is biomedical research, which a JHM IRB will review when the PI is from a Homewood Division. Homewood PIs whose research is biomedical in nature should contact HIRB for referral to a JHSPH IRB or JHM IRB, respectively. Also, when research is conducted within JHM, for instance at the Kennedy Krieger Institute, by a Homewood PI, the Homewood PI should contact HIRB before submitting an IRB application, as they may be told that JHM IRB must serve as the IRB of Record.

Collaborating Investigators with IRBs

Homewood faculty and staff may collaborate on research projects with investigators from non-JHU institutions that have their own IRBs. Homewood faculty and staff may act as PIs, investigators, or consultants and HIRB must exempt or approve the research regardless of where it takes place, unless another IRB serves as the IRB of Record (see below). For instance, HIRB and IRB approval from the collaborating institution(s) are required in the following situations:

- A Homewood faculty or staff member serves as a consultant on a human participant research project headed by a PI at another institution.
- A Homewood faculty or staff member collaborates with investigators from several other universities on a research project involving human participants.

IRB of Record. HIRB may, upon request from a PI with a primary appointment in one of the Homewood Divisions and with HIRB approval, serve as the IRB of Record for collaborating investigators who belong to institutions with their own IRB(s). This requires the HIRB Director to file a formal Authorization Agreement with OHRP. HIRB will also consider requests from Homewood investigators to delegate review responsibility to another IRB, usually the PI's IRB, when the PI of the project is not a member of the Homewood Divisions. The terms and conditions of these arrangements are negotiated by the HIRB Office, which can provide further details.

Multi-site studies. When investigators from multiple institutions with their own IRBs collaborate in a multi-site study, generally each should rely on his or her own IRB, and authorization agreements should not be used. HIRB must be provided with evidence of all collaborating investigators' IRB approvals. HIRB will grant only provisional approval of a research project before it obtains evidence of approval, provisional or final, from the IRBs of all collaborating investigators.

Collaborating Individual Investigators Without IRBs

Individual Investigator Agreements may be used by HIRB to cover collaborating individual investigators who are not associated with an IRB.

There are two types of collaborating individual investigators:

1. A *collaborating independent investigator* is (1) not otherwise an employee or agent of the Homewood Divisions; (2) conducting collaborative research activities outside the facilities of the Homewood Divisions; and (3) not acting as an employee of any institution with respect to his or her involvement in the research being conducted by the Homewood Divisions.
2. A *collaborating institutional investigator* is (1) not otherwise an employee or agent of the Homewood Divisions; (2) conducting collaborative research activities outside the facilities of the Homewood Divisions; (3) acting as an employee or agent of a non-assured institution (i.e., institution without an OHRP-approved IRB) with respect to his or her involvement in the research being conducted by the Homewood Divisions; and (4) the non-assured institution does not routinely conduct research involving human participants.

OHRP permits the Homewood Schools to extend its FWA to cover a collaborating independent or institutional investigator provided all of the following conditions are satisfied:

- The non-assured institution and HIRB approve the extension of the Homewood Schools' FWA through an Individual Investigator Agreement.
- The extension of the coverage of the FWA is put in place by use of an appropriate written agreement, such as OHRP's Individual Investigator Agreement, for each collaborating individual investigator who will be engaged in the research being conducted by the Homewood Schools. The assured institution must maintain the Individual Investigator Agreement on file and provide copies to OHRP upon request.
- For the collaborating institutional investigator, the appropriate authorities at the non-assured institution state in writing that the conduct of the research is permitted at their institution.
- A Homewood PI directs and appropriately supervises all of the collaborative research activities to be performed by the collaborating individual investigator outside JHU.
- The following documents are made available to the collaborating individual investigator: (a) *The Belmont Report*, (b) the DHHS regulations for the protection of human research participants [45 CFR 46], (c) the Homewood Schools' FWA and its applicable terms, and (d) HIRB policies and procedures for the protection of human research participants.
- The collaborating individual investigator understands and accepts the responsibility to comply with the standards and requirements stipulated in the documents referenced in the preceding paragraph and to protect the rights and welfare of human participants involved in research conducted under the Individual Investigator Agreement.
- The collaborating individual investigator agrees to comply with all other applicable Federal, state, local, and international laws, regulations, and policies that may provide additional protections for human participants in research conducted under the Individual Investigator Agreement.
- The collaborating individual investigator agrees to abide by all determinations of HIRB designated under the Homewood Schools' FWA and agrees to accept the final authority and decisions of HIRB, including but not limited to directives to terminate participation in designated research activities conducted under the Individual Investigator Agreement.

- The collaborating individual investigator agrees to complete the educational training required by HIRB of investigators prior to initiating research covered under the Individual Investigator Agreement.
- The collaborating individual investigator agrees not to enroll participants in research under the Individual Investigator Agreement prior to HIRB review and approval of the research.
- The collaborating individual investigator agrees to report promptly to HIRB any proposed changes in the research conducted under the Individual Investigator Agreement. The collaborating individual investigator agrees not to initiate changes in the research without prior HIRB review and approval, except where necessary to eliminate apparent immediate hazards to participants.
- The collaborating individual investigator agrees to report immediately to HIRB any unanticipated problems involving risks to participants or others in research covered under the Individual Investigator Agreement.
- The collaborating individual investigator, when responsible for enrolling participants, agrees to obtain, document, and maintain records of informed consent for each participant or the participant's legally authorized representative (LAR) as required by Federal regulations and HIRB policies and procedures.
- The collaborating individual investigator acknowledges and agrees to cooperate with HIRB in its initial and continuing review, record keeping, reporting, and certification for the research covered by the Individual Investigator Agreement. The collaborating institutional investigator agrees to provide all information requested by HIRB in a timely fashion.

Statistical and Coordinating Centers

Statistical and coordinating centers typically are responsible for overall data management, monitoring, and communication among multiple sites participating in a research project, as well as for general oversight of the conduct of the project. Statistical and coordinating centers may be designated either by a sponsor or by mutual agreement of the participating sites.

There are two possible ways to address statistical and coordinating centers located in the Homewood Schools or headed elsewhere by a Homewood PI.

1. The statistical or coordinating center PI will submit a specific protocol to HIRB that outlines the responsibilities of the center. It will not include local site protocol information, even if data are going to be collected by the same PI and/or other Homewood Schools' investigators, in which case a separate application for the local site will be submitted. The statistical or coordinating center protocol must be submitted to HIRB for review and approval prior to the initiation of center activities.
2. A Homewood Divisions PI will serve as the statistical or coordinating center PI and as the PI for a local site in a multi-center study. There will be a local site protocol that describes the study into which participants will be enrolled, and a specific statistical or coordinating center protocol will not be submitted. Instead, the statistical or coordinating center functions will be described in the local site protocol and consent documents. HIRB will review these documents to determine if the center functions are adequately described.

In either case, investigators must provide HIRB with a description or evidence of *all* of the following items:

- Each participating site's local IRB approval and consent documents.
- Each site's OHRP-approved FWA.
- The method for assuring that all sites have the most current version of the protocol.
- The plan for collection and management of data at all sites and the center.
- The system used to communicate amendments to the protocol to all sites.
- The process for reporting and evaluating adverse events and protocol deviations at all sites and the center.

Homewood Personnel Assisting Non-JHU PIs

Occasionally Homewood personnel may assist a non-JHU PI with a research project. Before Homewood personnel become engaged in research, which according to Federal policy occurs when Homewood employees or agents intervene or interact with living individuals for research purposes or obtain individually identifiable private information for research purposes, they must obtain HIRB approval or exemption of the research project. This is a Federal requirement. Please contact the HIRB Office for more information if needed. (Also see Section 5.1 through 5.3 for more details on engagement in research.)

Applicable Regulations & Guidelines

21 CFR 50, 56, 312, & 812

45 CFR 46

OHRP (January 6, 2005). *Federalwide Assurance (FWA) for the Protection of Human Subjects*.

OHRP (January 31, 2005). *Guidance on Extension of an FWA to Cover Collaborating Individual Investigators and Introduction of the Individual Investigator Agreement*.

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Section Two: HIRB Authority & Operation
Date of Revision: 11/17/14

Introduction

According to Federal policy, an institution holding a Federalwide Assurance (FWA) must certify that the institution's human participant research, unless exempt, is initially reviewed and approved by an IRB and undergoes continuing review at least annually. HIRB acts on behalf of the Homewood divisions it serves to review human participant research regardless of the funding source, lack of funding, or site at which the research is performed in order to ensure compliance with Federal, state, and local laws and regulations and institutional policies and procedure.

HIRB is an essential component of the Homewood Human Research Protection Program (HRPP), which subsumes the protections that are in place throughout the Homewood Divisions to ensure the rights and safety of human research participants. The Institutional Official (IO) is ultimately responsible for ensuring institutional compliance with all applicable provisions of the Federal regulations and the Homewood Schools' FWA.

Section Objective

The purpose of this section is to describe the authority by which HIRB operates; identify the roles and responsibilities of HIRB personnel; and provide an overview of the operation of HIRB, including brief descriptions of meetings, the review process, reporting, and oversight activities.

Relevant Definitions

APPROVAL Authorization by an IRB, after review of a research project, that permits the project to be conducted at an institution within the conditions set forth by the IRB and in accordance with Federal regulations and other institutional requirements. [45 CFR 46.102]

AUDIT Process by which HIRB examines a previously reviewed research protocol and research activities to date in order to ensure the continued protection of research participants and compliance with Federal, state, and local laws and regulations and HIRB policies and procedures.

EXEMPT REVIEW Review to determine if a study is minimal risk and falls into one of six categories identified in Federal regulations as potentially exempt [45 CFR 46.101]. Studies deemed exempt by HIRB are released from compliance with Federal regulations [45 CFR 46] at HIRB's discretion. Investigators are nevertheless required to treat participants ethically.

EXPEDITED REVIEW Review of proposed human participant research by the HIRB chair or one or more designated voting members instead of the full board. Federal rules permit expedited review for certain categories of research involving no more than minimal risk and for minor changes in ongoing research the IRB has previously approved [45 CFR 46.110].

FEDERALWIDE ASSURANCE (FWA) A written, binding commitment submitted to OHRP by an institution engaged in human participant research in which the institution promises to comply with applicable Federal regulations governing such research and specifies the procedures it will follow to ensure compliance [45 CFR 46.103]. The Johns Hopkins University Homewood Schools' Federalwide Assurance is No. 00005834.

FULL BOARD REVIEW Review of a proposed human participant research project at a convened IRB meeting at which a majority of members is present, including at least one member whose primary concerns are not scientific. A majority of those present must approve the research for it to receive IRB approval [45 CFR 46.108].

HRPP (HUMAN RESEARCH PROTECTIONS PROGRAM) The array of protections that are in place throughout the Homewood Divisions to ensure the rights and safety of human participants in research associated with the divisions.

INSTITUTIONAL OFFICIAL (IO) The IO has ultimate responsibility for the institutional commitment made in HIRB's Federalwide Assurance (FWA). The IO is authorized to assure HIRB complies with the terms of the FWA and is ultimately responsible for the review and oversight of human participant research conducted in association with or supported by the Homewood Divisions. The IO cannot be an IRB member or chairperson.

INSTITUTIONAL REVIEW BOARD (IRB) A specially constituted review body recognized by the Office for Human Research Protections (OHRP) of the Department of Health and Human Services (DHHS) to protect the welfare of human participants in behavioral or biomedical research at a specific institution [45 CFR 46.102, 108, & 109].

OHRP (OFFICE FOR HUMAN RESEARCH PROTECTIONS) OHRP is an administrative office within the Department of Health and Human Services (DHHS). OHRP implements Federal regulations for the protection of human research participants [45 CFR 46] and provides guidance on ethical issues in biomedical and behavioral research.

QUORUM A majority of the IRB voting members, including at least one member whose primary concerns are in nonscientific areas. At IRB meetings, a quorum must be established and maintained for the deliberation and vote on all matters needing full board approval.

2.1 HIRB Authority

HIRB derives its authority from both regulatory and institutional sources. HIRB functions according to its written Standard Operating Policies and Procedures, which comply with the obligations of the Homewood Schools' FWA. The FWA is a written, binding commitment made by the JHU Homewood Schools to OHRP to comply with applicable Federal regulations governing human participant research. HIRB is required to review and has the authority to (1) exempt, approve, require revisions of, or disapprove all human participant research under its purview, including proposed changes in ongoing, previously approved research, and (2) suspend or terminate the approval of human participant research that is not being conducted in accordance with Federal, state, or local laws or regulations or HIRB policies and procedures or that has been associated with unanticipated harm or risk to participants or others.

2.2 Institutional Official (IO)

The Institutional Official (IO) for the Homewood Schools has ultimate responsibility for the institutional commitment made in the Homewood Schools' Federalwide Assurance (FWA). The IO is authorized to ensure that HIRB complies with the terms of the FWA, including Federal regulations for the protection of human research participants, and is ultimately responsible for the review and oversight of human participant research conducted or supported by the Homewood Divisions. The IO also serves as the central authority for the Human Research Protections Program (HRPP) for the Homewood Schools.

The IO is directly responsible for the activities listed below:

- Possessing knowledge about the requirements of Federal, state, and local laws and regulations governing human participant research; the Homewood Schools' FWA; and HIRB policies and procedures for the protection of human research participants.
- Ensuring institutional compliance with all applicable provisions of the Homewood Schools' FWA and Federal regulations governing the protection of human research participants.
- Serving as a knowledgeable contact for OHRP.
- Reporting to OHRP any serious or continuing noncompliance with Federal regulations.
- Reporting to OHRP any suspension or termination of HIRB approval of research.
- Setting an organizational tone for the Homewood Divisions that fosters a culture of respect for human research participants.
- Ensuring interdivisional communication and guidance on human participant research.
- Having authority to speak on behalf of the Homewood Divisions with regard to HIRB and its functions.
- Identifying and appointing (in consultation with the HIRB Chair, HIRB Director, and Department Chair, when applicable) appropriate faculty and community members to serve as HIRB members.
- Supporting the authority and decisions of HIRB.
- Completing the OHRP training module.

The IO also has oversight responsibility for the activities listed below:

- Monitoring compliance with Federal, state, and local laws and regulations.
- Educating the research community (faculty, students, and staff) in order to establish and maintain maximum compliance with HIRB policies and procedures and Federal regulations governing the protection of human research participants.
- Developing and updating HRPP and HIRB policies and procedures.
- Ensuring that personnel reviewing, conducting, or supporting human participant research are sufficiently cognizant of human research participant protections.

2.3 HIRB Personnel

HIRB personnel include the HIRB Chair, board members, the Director, and office staff. All personnel are required to complete IRB training and to possess knowledge of and comply with the requirements of Federal, state, and local laws and regulations governing human participant research, the Homewood Schools' FWA, and HIRB policies and procedures for the protection of human research participants.

HIRB Members

The members of HIRB represent the academic disciplines in the Homewood Divisions, as well as community views and attitudes and nonscientific perspectives. The membership has appropriate knowledge of the settings in which the divisions' research typically is performed. As required by Federal regulations, HIRB is sufficiently qualified — through its members' experience; expertise; diversity in race, gender, and cultural background; and sensitivity to community attitudes — to engender respect for its advice and counsel. These assets are utilized when HIRB reviews applications for approval of research involving human participants. HIRB is able to evaluate the acceptability of proposed research in terms of institutional policies and procedures; Federal, state, and local laws and regulations; and standards of professional conduct and practice.

HIRB is comprised of at least five faculty members, including the Chair, with expertise in diverse discipline areas. The board also includes at least one member whose primary concerns are nonscientific and one member who represents the community. The HIRB Office maintains records of the qualifications of all HIRB members. Individuals with competence in special areas may be invited to assist in review of individual applications; these consultants may not, however, vote on the applications.

The Institutional Official appoints HIRB members in consultation with the HIRB Chair, the HIRB Director, and the Department Chair, when appropriate. Periods of service are three years for faculty members and indefinite for community members.

HIRB Chair

The Institutional Official appoints the HIRB Chair in consultation with the HIRB Director. The Chair's responsibilities include the following:

- Participating in the development of HRPP and HIRB policies and procedures.
- Reviewing new research applications, requests for amendments and changes, and progress reports for continuing review.
- Designating HIRB members as expedited reviewers.
- Presiding over and facilitating HIRB full committee meetings.
- Presenting a primary reviewer's findings and recommendations when the reviewer is unable to attend the HIRB full committee meeting at which the review has been scheduled.
- Reviewing reports of unanticipated problems.
- Corresponding with investigators on behalf of HIRB, as necessary.

- Reviewing allegations of investigator noncompliance and complaints regarding research and ensuring, in consultation with the full HIRB committee, that they are properly investigated and resolved.

HIRB Director

The HIRB Director is the administrative coordinator of the HIRB review process and plays an important role in communicating HRPP and HIRB policies and procedures to faculty, students, and staff. The Director is responsible for ensuring that administrative policies and procedures related to the ethical review of human participant research are consistently carried out. Additionally, the Director is the central person in the HIRB Office who oversees compliance with Federal, state, and local laws and regulations and HIRB policies and procedures. The HIRB Director is directly responsible for the following activities:

- Serving as a knowledgeable point of contact for OHRP.
- Ensuring that all collaborating institutions have appropriate OHRP-approved assurances.
- Identifying and addressing potential vulnerabilities in achieving compliance in research studies by working closely with various JHU offices, such as the Research Projects Administration Office and the Office of General Counsel, and preparing reports to appropriate institutional officials and HIRB.
- Possessing knowledge about the requirements of Federal, state, and local laws and regulations, the Homewood Schools FWA, and HIRB policies and procedures for the protection of human participants.
- Complying with all applicable provisions of the Homewood Schools' FWA.
- Serving as a resource for the HIRB Chair and members, HIRB Office staff, and investigators on regulatory issues that arise in the review and conduct of human participant research.
- Managing and revising HIRB policies and procedures.
- Determining, on behalf of HIRB, whether research qualifies as exempt from Federal regulations for the protection of human research participants.
- Performing expedited review of minor changes (administrative changes, minor revisions, word for word modifications, etc.) to initial applications, continuing review, and amendments that meet the criteria for expedited review.
- Signing off on review of minor requests by the primary reviewer.
- Performing review of new applications, continuing review, and amendments which meet the criteria for expedited review in role as voting IRB member,
- Performing for-cause audits of research projects at the instruction of the HIRB or HIRB Chair.
- Facilitating interdivisional communication and guidance on human participant research.
- Educating faculty, students, and staff on behalf of HIRB on issues related to the protection of human research participants.

- Monitoring HIRB Office performance.

The HIRB Director has oversight responsibility for the activities listed below:

- Coordinating HIRB full committee meetings and ensuring that a majority of the HIRB members is present, including at least one nonscientist.
- Ensuring that changes in approved research are not initiated without prior HIRB approval.
- Ensuring the prompt reporting to HIRB, the Institutional Official, OHRP, and other appropriate agencies of any unanticipated harm or risk to participants or others; any serious or continuing noncompliance with Federal, state, or local laws or regulations or HIRB policies and procedures, including failure to comply with HIRB determinations; and any suspension or termination of HIRB approval.
- Maintaining copies of all reviewed research protocols, scientific evaluations, approved sample consent documents, requests for changes, progress reports for continuing review, reports of unanticipated problems, Certificates of Confidentiality, and correspondence between HIRB and investigators.
- Maintaining file copies of all HIRB meeting minutes.
- Ensuring that appropriately maintained HIRB records and correspondence are available upon request to authorized Federal officials.

HIRB Office Staff

The HIRB Office requires trained staff who possess knowledge of the Federal, state, and local laws and regulations governing human participant research, the Homewood Schools' FWA, and HIRB policies and procedures for the protection of human research participants. Office staff members are responsible for the administrative review of all HIRB submissions that involve human research participants. Office staff members are selected and supervised by the HIRB Chair and Director.

The HIRB Office staff is directly responsible for the activities listed below:

- Possessing knowledge of and complying with the requirements of Federal, state, and local laws and regulations, the Homewood Schools' FWA, and HIRB policies and procedures for the protection of human research participants. This should be fostered through professional development, such as certification, and participation in professional associations.
- Ensuring that all collaborating institutions have appropriate OHRP-approved assurances.
- Preparing regular and periodic performance reports on HIRB activities for Homewood administrators and faculty.
- Initiating and/or composing routine correspondence to investigators.
- Maintaining a dialogue with faculty, staff, and student investigators to support their preparation and submission of protocols for review that accord fully with ethical and regulatory requirements.
- Monitoring compliance with relevant Federal regulations.
- Screening protocols before HIRB review.

- Assigning protocols to HIRB members for expedited review.
- Reviewing amendments regarding change of research team members on previously approved research protocols.
- Providing administrative support for HIRB full committee meetings.
- Ensuring that a quorum of HIRB members is present, including at least one nonscientist, at all HIRB full committee meetings.
- Ensuring that HIRB meeting minutes include attendance; HIRB actions; the votes on these actions, including the number voting for, voting against, and abstaining; when members leave the meeting due to a conflict of interest; the basis for requiring revisions or disapproving of research; documentation of specific findings as required by Federal regulations; and a summary of the discussion of controverted issues and their resolution.
- Maintaining file copies of all HIRB meeting minutes.
- Ensuring HIRB records and correspondence are maintained appropriately and available upon request to authorized Federal officials.

2.4 HIRB Consultants

The members of HIRB possess a broad range of scientific expertise and knowledge of the local research context. Occasionally the members do not have sufficient expertise to evaluate the scientific merit of a proposed study or adequate knowledge of the research context, such as when the research will be conducted at an international site. When the HIRB Director and/or Chair determines that outside expertise is needed to evaluate a research project adequately, a consultant will be called upon to assist HIRB. The consultant may be asked to provide a written and/or oral scientific evaluation to HIRB, attend a HIRB board meeting to answer questions, or answer specific questions posed by the Director or Chair. The consultant is not permitted to vote on whether to approve the research.

2.5 HIRB Meetings

HIRB full committee meets on an as-needed basis for full committee review of new research applications, continuing review applications, requests for amendments and changes, and reports of unanticipated problems. Full committee meetings require that a majority of voting members, or a quorum, be present, including at least one nonscientist. If the required number of members or nonscientist is lost during a meeting, no action may be taken until a quorum is restored. In order for research requiring full board review to be approved, it must receive the approval of a majority of the voting members present at the meeting.

HIRB may, at its discretion, ask investigators to present their applications at a convened HIRB meeting. When this happens, the investigators must leave prior to HIRB deliberations and voting.

Attendance at convened HIRB meetings is limited to HIRB members, HIRB staff, invited investigators, consultants, and guests. Meeting proceedings are confidential. Minutes are kept of each full committee meeting. The minutes include a list of attendees; actions taken by HIRB; the vote on these actions, including the number of members voting for, voting against, and abstaining;

the basis for requiring revisions of or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

2.6 HIRB Member Conflicts of Interest

A HIRB member may not participate in the review of any study in which he or she has a conflicting interest, except to provide information requested by other HIRB members or staff. At the beginning of each meeting, members are asked to declare if they have a conflict, financial or otherwise, with the research to be reviewed and reminded to recuse themselves at the time of review. The HIRB meeting minutes will note the recusal when it occurs.

2.7 HIRB Review

There are three levels of review for human participant research: (1) exempt, (2) expedited, and (3) full board. The HIRB Director is the authority for determining whether a research project qualifies as exempt. The HIRB chair or one or more HIRB members conduct expedited reviews on an ongoing basis. Human participant research that does not qualify as exempt or for expedited review is reviewed by the full board at a HIRB meeting. HIRB conducts continuing reviews of ongoing, previously approved research at predetermined intervals appropriate to the studies' degree of risk but no less frequently than once per year.

The criteria for HIRB approval of research must include all of the determinations listed below:

- Risks to participants are minimized.
- Risks are reasonable in relation to anticipated benefits.
- Selection of participants is equitable.
- Informed consent is sought from each participant (unless HIRB waives the informed consent requirements).
- Informed consent is appropriately documented (unless HIRB waives documentation of informed consent).

Where appropriate, the criteria for HIRB approval may also include the following determinations:

- Data collection is monitored to ensure participant safety.
- Privacy and confidentiality of participants is protected.
- Additional safeguards are included for vulnerable populations.

2.8 HIRB Reports

HIRB decisions as to whether to approve, require revisions, or disapprove human participant research are communicated to investigators in writing. The only individuals authorized to discuss substantive aspects of the Committee's review and determinations with investigators are the HIRB Chair, HIRB members who reviewed the study, invited consultants, the HIRB Director, and designated HIRB staff.

2.9 HIRB Monitoring Activities

HIRB is responsible for ensuring that investigators are monitored and research is conducted as approved by HIRB and in accordance with the Homewood Schools' FWA. This includes ensuring that changes in approved research, during the period for which approval has been granted, are not initiated without prior HIRB approval. Additionally, HIRB is responsible for resolving complaints regarding research from research participants, investigators, staff, and others. In its monitoring role, HIRB performs or oversees routine, random, and targeted audits to ensure compliance with Federal regulations and HIRB policies and procedures.

Continuing Review

Investigators are required to submit progress reports for continuing review no less frequently than annually for nonexempt research. For continuing review, HIRB evaluates whether the research is being conducted according to the approved protocol; evaluates investigators' summaries of unanticipated problems, adverse events, and complaints; and assesses whether the risk/benefit ratio has changed and new protections are needed.

Random Audits

HIRB Office staff may conduct random audits of approved research projects in order to ensure that projects are in compliance with Federal regulations and HIRB policies and procedures. HIRB Office staff also may audit exempted studies to ensure that they continue to meet the requirements for exemption. Random audits may include:

- Examination of investigator research records.
- Observation of the informed consent process.
- Observation of data collection.
- Confirmation from sources other than the investigators, such as research staff and participants, that no substantial changes in the research protocol have occurred without prior HIRB review and approval.

For-Cause Audits

HIRB may conduct or instigate a for-cause audit of research suspected to be in noncompliance with Federal regulations or HIRB policies and procedures, including research that is not being carried out as approved by HIRB. Targeted audits may result from complaints received from a participant, evidence of deviation from the approved protocol in a progress report submitted for continuing review, or another trigger. The HIRB Chair may order the audit, or it may be passed as a motion by the full board. HIRB may request that an individual from the Office of General Counsel or a JHU Compliance Officer conduct the review and report his or her findings to HIRB. The audit may involve and is not limited to interviews with research team members and participants; observations of study procedures, including the informed consent process; and examination of study records.

HIRB Actions Following Audits

When an audit reveals minor noncompliance with Federal regulations or HIRB policies and procedures, HIRB board members and staff will work with investigators to bring the project back into compliance. If the noncompliance is serious (i.e., the rights or welfare of research participants is

negatively affected or in jeopardy) or cannot be easily resolved, the matter will be reported to the full board, and procedures for serious and continuing noncompliance will be followed. In response to serious or continuing noncompliance, HIRB may suspend the study, withdraw approval for the study, or take other actions necessary to protect the rights and welfare of research participants.

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Section Three: Investigator Responsibilities
Date of Revision: 11/17/14

Introduction

PIs and other investigators are responsible for how human participant research is planned and conducted. This responsibility begins with the design of the research protocol, is followed by interactions with HIRB and the actual conduct of the research, and ends with the study's closure. A fundamental responsibility of all investigators engaged in human participant research is the protection of the rights and welfare of study participants.

Section Objective

This section focuses on investigator responsibilities, particularly with respect to the protection of research participants' safety and data confidentiality. Investigator qualifications and responsibilities are described, investigator conflicts of interest are addressed, information about Certificates of Confidentiality is provided, and data safety and monitoring requirements are covered.

Relevant Definitions

CERTIFICATE OF CONFIDENTIALITY A document issued by the National Institutes of Health (NIH) and other HHS agencies that provides protection against compelled disclosure (e.g., subpoena) of names and other identifying information about participants enrolled in sensitive biomedical, behavioral, clinical, or other research, including research on mental health and the use and effect of alcohol and other psychoactive drugs. Certificates are not limited to Federally supported research.

CONFIDENTIALITY Refers to the privacy of human research participants and efforts to control access to information related to their participation in order to protect their privacy.

DATA SAFETY MONITORING BOARD (DSMB)/SAFETY MONITORING COMMITTEE (SMC) A group of scientists, physicians, bioethicists, statisticians, and other experts that collects and analyzes data during the course of a research project involving greater than minimal risk. The group monitors data for adverse effects and other trends (such as an indication that one treatment is significantly better than another, particularly when one arm of a trial involves a placebo control) that would warrant modification or termination of the study or notification of the participants about new information that might affect their willingness to continue in the study. The group also monitors the confidentiality of participants' data to ensure their privacy.

DATA SAFETY MONITOR (DSM) A scientist, physician, bioethicist, statistician, or other expert who collects and analyzes data during the course of a research project involving greater than minimal risk. The individual monitors data for adverse effects and other trends that would warrant modification or termination of the study or notification of the participants about new information that might

affect their willingness to continue in the study. The DSM also monitors the confidentiality of participants' data to ensure their privacy.

3.1 Investigator Qualifications

PIs of research projects approved by HIRB must be full-time, adjunct, or emeritus members of the faculty or designated senior staff members in one of the divisions covered by the JHU Homewood Schools' Federalwide Assurance (FWA). The reason for this stipulation is that faculty and senior staff members are required to know the policies of JHU and can be held accountable for the conduct of human participant research approved by HIRB. PIs must sign applications submitted to HIRB for initial protocol review, continuing review, amendments and changes, and study closure, as well as reports of unanticipated problems and data safety and monitoring activities.

Students cannot serve as PIs. Students who wish to conduct research with human participants must enlist a faculty member, typically their faculty advisor, to serve as the PI. The student is considered the co-investigator. The faculty PI is expected to work closely with the student in preparing applications for HIRB review, overseeing the proper conduct of the research, and ensuring that the study is appropriately closed upon completion.

All investigators — the PI and others — involved in the conduct of human participant research must be adequately qualified, given the scope and complexity of the study, to conduct the research in order for HIRB to grant approval. The addition of investigators following HIRB's initial approval of a nonexempt study must be approved by HIRB prior to the investigators' involvement with participants or participants' data. Such approval can be requested in an amendment or continuing review application submitted by the PI.

As specified below and in Section 4, all investigators planning to conduct human participant research are required to complete training in the ethical conduct of human participant research. The PI, investigators, and other key study personnel who are listed on the initial application must complete this training prior to submission of the application to HIRB for approval or exemption. Investigators and other key personnel who wish to join a nonexempt study following HIRB's initial approval of the research protocol must complete their training before the PI requests their addition to the research team. These rules apply regardless of whether the research is funded or unfunded and irrespective of the funding source or where the research is conducted.

3.2 General Responsibilities

PIs are directly and primarily responsible for ensuring the protection of every individual who takes part in their research. All proposed human participant research for which Homewood faculty or senior staff members are PIs must be submitted to HIRB for review and approval or exemption, unless a reciprocity or authorization agreement is in place for another IRB to review the research, as is the case for prisoner and biomedical research. PIs whose primary appointment is in another (non-Homewood) JHU institution generally should submit their research for review at that institution. PIs who conduct nonexempt human participant research are responsible for all of the tasks listed below.

Conduct of the Research

- Obtaining HIRB approval prior to commencing any human participant research — this includes consulting with HIRB Office staff if there is any doubt as to whether the activity qualifies as human participant research, which must be reviewed by an IRB.

- Complying with all applicable provisions of the Homewood Schools' FWA.
- Disclosing all actual or perceived conflicts of interest regarding their research.
- Conducting research according to the HIRB-approved protocol.
- Ensuring that risks to participants are minimized, risks are reasonable in relation to anticipated benefits, and the selection of participants is equitable.
- Ensuring that informed consent is sought from each participant, using a HIRB-approved consent form or procedure, and that the consent is appropriately documented, unless HIRB has waived the consent requirements or documentation.
- Ensuring that data collection is monitored to ensure participant safety and confidentiality of the data.
- Ensuring that additional safeguards are in place for vulnerable populations.
- Submitting all proposed changes to previously approved protocols to HIRB for review and approval and ensuring that changes to approved research are not initiated without prior HIRB approval, unless they are necessary to eliminate immediate hazards to participants.

Record Keeping and Reporting

- Ensuring that all research records and correspondence are maintained appropriately and are available upon request to authorized Federal officials and JHU auditors. All research-related records, including records of IRB activities and research records held by investigators, must be kept for at least three years after completion of the research (45 CFR 46.115(b)). All study documents for protocols involving minors (individuals under the age of 18), or *both* minor and adult participants must be maintained until the youngest individual enrolled in the study is 18 years old, or for three years following completion of the study, whichever is longer.
- Ensuring prompt submission of proposed changes to HIRB for review and approval.
- Ensuring prompt reporting to HIRB and appropriate agencies of unanticipated problems that harm or create risks for research participants or others.
- Maintaining copies of all research protocols reviewed, scientific evaluations, approved sample consent documents, progress reports for continuing review, reports of unanticipated problems (which include injuries to participants), data safety and monitoring reports, and correspondence between investigators and HIRB.
- Maintaining all signed consent documents in the manner approved by HIRB.
- Submitting progress reports to HIRB on the schedule set by HIRB for continuing review, which must occur at least annually.
- Complying with state-required (or, in the case of international research, nationally- or locally-required) mandatory reporting of specified diseases and conditions.
- Accounting for any disclosure of protected health information.

Monitoring and Oversight

- Monitoring compliance with Federal regulations for the protection of human research participants throughout the duration of the project.
- Ensuring that all collaborating performance sites that are engaged in research have appropriate OHRP-approved assurances.
- Ensuring that all research performance sites have and can document appropriate mechanisms to protect research participants.

Communication

- Complying with all research record keeping and reporting requirements.
- Ensuring that each potential research participant understands the nature of the research, taking all necessary steps to achieve that understanding, including communication of associated risks and benefits, and ensuring that participation is voluntary.
- Providing a copy of the signed HIRB-approved informed consent document to each participant at the time of consent, unless HIRB waives this requirement.

Education and Training

- Ensuring that all personnel involved in carrying out the research project demonstrate sufficient knowledge of the protection of research participants, which requires that all investigators and research staff (including students) complete the training required by HIRB on the protection of human research participants prior to taking part in the research. (See Section 4 for more details.)
- Ensuring that investigator(s) and research team members (including students) have sufficient scientific expertise to conduct the research.
- Possessing knowledge of Federal, state, and local laws and regulations governing human participant research, the Homewood Schools' FWA, and institutional policies and procedures for the protection of human research participants.
- Being sufficiently educated to establish and maintain thorough compliance with Federal regulations and institutional policies and procedures relevant to the protection of human research participants.

3.3 Investigator Conflicts of Interest

Financial interests in human subjects research require additional scrutiny. Such interests may present real or perceived risks to the welfare and rights of human subjects, in addition to presenting risks to research integrity. It is presumed that individuals (faculty, staff, trainees, students, administrators, and researchers) may not participate in research projects involving human subjects that are greater than minimal risk while they have a significant financial interest in the research project or in a financially interested company. Exceptions may be made in specific cases when, in the judgment of the IRB, individuals holding significant conflicting financial interests provide the IRB with a compelling justification – consistent with the rights and welfare of human research subjects for being permitted to simultaneously hold the financial interest and participate in the human subjects research project.

Protocol applications submitted to the Johns Hopkins University Institutional Review Boards include a question concerning relevant financial interests. If a covered party, including any research team member or immediate family member of a research team member, has a relevant financial interest, the question on the application must be answered in the affirmative. All protocol applications containing an affirmative answer to the question concerning relevant financial interests will be reviewed by the IRB and referred to the Conflict Review Committee for review as needed. The Conflict Review Committee reviews information related to all financial and/or fiduciary arrangements in light of related research activity. In its review, the Committee considers the following factors:

- a) impact on the integrity of research data;
- b) risks to the rights and safety of human research subjects
- c) risks to the rights and obligations of students and trainees participating in research;
- d) impact on the availability of research results to the scientific community for use in the public interest;
- e) appearance of a conflict of interest

Upon completing its review, the Committee will recommend to the appropriate Dean that the proposed arrangements be either prohibited or permitted, subject to specific management conditions. After reviewing the recommendation of the Committee, the Dean will render a final decision and will communicate that decision, with a description of any specific management conditions, to the involved covered party in writing. The Dean shall report his decision in each case to the IRB and the Conflict Review Committee.

3.4 Data Safety and Monitoring

According to Federal regulations, investigators' research protocols, when appropriate, should (1) make adequate provisions for monitoring collected data to ensure the safety of research participants and (2) include adequate provisions to protect participants' privacy and maintain data confidentiality.

All research protocols, except those for exempt research, must include description of the extent to which and how the confidentiality of records identifying participants, including records that reveal participation in the study, will be maintained throughout and after completion of the study. The provisions must be appropriate given the nature of the research and the risk posed by any release of identifying information and possible breaches of confidentiality. Investigators may need a Certificate of Confidentiality to protect them from having to release potentially incriminating or compromising information about research participants, as in the event of being served a subpoena (see Section 2.7). Federal regulations require that provisions, if any, for confidentiality be explicitly communicated to participants during the informed consent process and in consent forms, unless waived by HIRB.

When changes to the research protocol or the informed consent process or documents are needed to improve participants' safety and the confidentiality of their data, the PI should provide the rationale for the changes and request HIRB approval to implement them. Changes cannot be made without HIRB approval unless needed to protect participants from immediate hazards.

Progress reports submitted to HIRB for continuing review, which must occur at least annually, should include a summary of all data safety and monitoring activities that have taken place during

the most recent period of approval. However, when research involves greater than minimal risk, investigators are required to do more than summarize data safety and monitoring activities in progress reports for continuing review.

When risks to participants in a proposed research study are greater than minimal, investigators must provide HIRB with a data safety and monitoring plan. This plan must include a description of how data will be analyzed during the data collection process. Such analysis potentially allows investigators to detect problems in the research design and discover unexpected risks to research participants prior to the study's conclusion. With HIRB approval, changes to the research protocol or consent process or forms can be introduced to remedy problems, reduce risks to participants, or more accurately inform participants of the risks. Investigators should also include ongoing review of study procedures related to confidentiality in their data safety and monitoring plan to protect the privacy of research participants and the confidentiality of their data.

Both the timing and adequacy of the plan for analysis and review of the data and procedures related to confidentiality are important. For instance, if the data are not analyzed and reviewed until the project's end, there is no opportunity to make mid-course corrections based on the data. The level of monitoring in the research plan should correspond with the study's degree of risk.

Data monitoring is particularly important in clinical trials, which are reviewed by a Johns Hopkins Medicine IRB, as per an authorization agreement. The IRB must verify that the progress of the clinical trial will be adequately monitored so that, over the course of the study, it can be determined whether information gleaned from the study or other related clinical trials changes the ratio of risks to benefits, needs to be passed on to participants, should alter the recruitment of participants, and/or necessitates modification or discontinuation of the treatment(s) being evaluated. Individuals independent from the research team should be responsible for monitoring clinical trials and making recommendations about modifications or discontinuation of the research.

Data Safety and Monitoring Plan Elements

All investigators whose research involves greater than minimal risk must submit a data safety and monitoring plan as part of their HIRB application for new research. Because plans can vary depending on the potential risks, size, and complexity of the research study, rigid policies have not been established, but investigators should address the following when composing their plan:

1. What individual (e.g., the PI, another study investigator, a DSM) or group (e.g., a DSMB or SMC) will be responsible for the data and safety monitoring?
 - The greater the risk, the more essential it is that the person responsible for data and safety monitoring is independent from the study.
 - If a DSM, DSMB, or SMC will be utilized, investigators should appoint the individual or members, who should be independent from the investigators and without apparent financial, professional, or other conflicts of interest. DSMB and SMC members should have relevant and diverse expertise and may be basic scientists, statisticians, bioethicists, epidemiologists, physicians, school psychologists, or other professionals. The appropriate number of members should be guided by the expertise needed.
2. What will be monitored? Monitoring may include but is not limited to the following:

- Evaluation of the progress of the study, including assessments of data quality and participant recruitment, accrual, and retention.
 - Reports of adverse events and unanticipated problems. (See Section 12 for more information.)
 - Review of both adverse event and outcome data to determine whether there is any change in the risk-benefit ratio for study participants and whether the study should continue as originally designed, be changed, or be terminated. (If appropriate, interim analyses of the efficacy of the intervention should be performed in accordance with previously defined stopping rules, which specify the timing of the analyses and the criteria for termination.)
 - Assessment of external factors or relevant information (e.g., pertinent scientific literature reviews, therapeutic developments, results of related studies) that may affect the safety of participants or the ethical operation of the study.
 - Review of study procedures designed to ensure the protection of participants' privacy and data confidentiality.
3. How frequently will monitoring occur?
 4. What information will be reported to HIRB? How frequently will HIRB receive reports?

Investigators should provide their rationale for the above elements, each of which is subject to HIRB review and approval.

3.5 Certificates of Confidentiality

Certificates of Confidentiality, issued by the National Institutes of Health (NIH) and other Department of Health and Human Services (DHHS) agencies, protect the confidentiality of information obtained from research participants. Certificates protect investigators and institutions from being compelled to release sensitive and identifiable information about research participants. Certificates thus help to achieve research objectives, promote participation in studies by assuring privacy to participants, and ensure that participants will not be harmed as a result of taking part in research. A Certificate does not, however, take the place of good data security or clear policies and procedures for data protection, which are essential to protect the privacy of research participants.

Certificates are issued for individual studies to the institution or university where the research will be conducted. Investigators who need Certificates for multiple studies must submit multiple applications. Exceptions are made for multi-site studies and coordinating centers. If a Homewood Division is the lead institution on a multi-site study or a coordinating center, the Homewood PI can apply for and receive a Certificate on behalf of all member institutions. The application must list each participating site with its address and project director. In addition, the lead site must indicate that it has on file a copy of IRB approval and IRB-approved consent form(s) from each site, which will be made available upon request to the agency granting the Certificate.

When a Certificate of Confidentiality Is Appropriate

A PI who plans a study in which sensitive and identifiable information will be obtained should consider applying to a DHHS agency for a Certificate. Sensitive information is data that, if disclosed, could damage participants' financial standing, employability, insurability, or reputation or have other

adverse consequences. Projects eligible for a Certificate include those that collect sensitive data on medical problems, including genetic abnormalities; participants' psychological states; participants' sexual attitudes, preferences, or practices; and illegal behaviors such as drug abuse.

Projects not eligible for a Certificate include those that are not research; do not collect personally identifiable information; are not reviewed and approved by an IRB; or collect information that, if disclosed, would be unlikely to significantly harm or damage participants. Investigators must justify their need for a Certificate.

Protections Afforded by a Certificate

Except as described below, Certificates allow an investigator and others who have access to research records to refuse to disclose identifying information in any civil, criminal, administrative, legislative, or other proceeding at the Federal, state, and local levels.

While Certificates protect against involuntary disclosure, participants may voluntarily disclose, or request investigators to disclose, their research data or information. Participants may, for example, authorize the investigator in writing to release the information to physicians, insurers, employers, or other third parties. In such cases, researchers may not use the Certificate to block disclosure.

Certificates do not authorize researchers to refuse to disclose information about participants if authorized DHHS or JHU personnel request such information for an audit or program evaluation. Nor can researchers refuse to disclose such information if it is required to be disclosed by the Federal Food, Drug, and Cosmetic Act.

Researchers are also not prevented from disclosure of child abuse, reportable communicable diseases, or a participant's threat of violence to self or others. Indeed, in certain situations, researchers are required to make disclosures regardless of a Certificate. If the researcher is required or intends to make such disclosures, this must be clearly stated in the consent form.

Mandatory Reporting Requirements

Researchers are expected to comply with state and local requirements to report communicable diseases and also to meet other mandatory reporting requirements, such as those for suspected child abuse. (For further guidance on required reporting, see Reportable Diseases and Conditions in Section 3.6.) Any researcher desiring *not* to comply with reporting requirements must justify the request to HIRB and obtain HIRB approval of the nondisclosure plan. Requests must be based on the welfare and rights of participants.

In the nondisclosure plan, the investigator must describe *one* of the following:

1. An agreement that the applicant has made with the health department to cooperate in ways that serve the purposes of communicable disease reporting requirements.
2. The specific reasons related to confidentiality requirements of the research that preclude such reporting.

When physicians conducting research also provide clinical care for the participants in a nonresearch relationship, the protections of the Certificate do not apply and those physicians are considered the referring physicians for purposes of this policy.

Requirements for Informed Consent

When a Certificate has been obtained, the consent form must inform participants that a Certificate of Confidentiality is in effect and must describe both the protections afforded by the Certificate and any limitations or exceptions to these protections. Investigators who have applied for or plan to apply for a Certificate must state in the consent form(s) submitted for HIRB review that a Certificate will be obtained and describe the protections afforded by the Certificate and their limitations. The Certificate should not be represented as an endorsement of the study by DHHS or used as a means of coercing recruitment of participants. If a Homewood Division is the lead institution on a multi-site study or a coordinating center and holds a Certificate for the collaborating institutions, the consent form(s) for each site must describe the protections and limitations of the Certificate.

Investigators who do not consider applying for a Certificate prior to HIRB review and approval but later apply for and obtain one must notify participants of the protections and limitations provided by the Certificate. This should be done by a consent addendum for already enrolled participants and a revised consent form that includes the appropriate language concerning the Certificate for new enrollees. The consent addendum and revised consent forms must be reviewed and approved by HIRB through submission of an Application for Amendments and Changes.

International Studies

If the data obtained from a study conducted outside the U.S. are maintained within the U.S., a researcher may utilize a Certificate. If the data are only maintained in a foreign country, a Certificate's legal protections are not effective.

Applying for a Certificate of Confidentiality

Usually applications for a Certificate of Confidentiality are submitted following HIRB approval of the research protocol. This is because Certificates are not issued unless IRB approval, or IRB approval conditioned on receipt of a Certificate, has been granted. Approximately three months should be allowed for receipt of the Certificate. Investigators may apply for a Certificate by completing the application found at the Certificates of Confidentiality Kiosk [<http://grants1.nih.gov/grants/policy/coc/>]. Investigators should review the instructions and other information concerning Certificates at the kiosk.

3.6 Reportable Diseases and Conditions

States mandate reporting of specific infectious diseases, outbreaks, and certain other conditions, such as child and elder abuse. HIRB recommends that investigators generally abide by the same reporting requirements as health care providers. The HIPAA Privacy Rule permits physicians and other covered entities to disclose protected health information, without a patient's written authorization, to public health authorities who are legally authorized to receive such reports for the purpose of preventing or controlling disease. Reportable diseases vary by state but are based on a national list that is prepared and periodically revised by the Centers for Disease Control.

Reportable Diseases

Maryland Code requires that reports by health care providers (and, by extension, researchers) of diseases and outbreaks be made in writing within 48 hours of discovery or, for certain conditions, immediately by telephone. Specific conditions that must be reported are listed on the Maryland

Department of Mental Health and Hygiene Web site [<http://www.edcp.org/html/reprtabl.html>]. Diseases and conditions that must be reported include:

- Any condition made reportable by department orders or new regulations (e.g., SARS, which is reportable by telephone).
- A single case of a disease of known or unknown etiology that may be a danger to the public health (reportable in writing).
- Unusual manifestation(s) of a communicable disease in an individual (reportable by telephone).
- Outbreaks of known or unknown etiology that may be a danger to the public health (reportable by telephone).

Reports should be made to the local health authority (the Commissioner of Health for Baltimore City and the respective County Health Officer for other Maryland counties). At a minimum, the report should include the disease or condition being reported; the name and address of the researcher or physician making the report; and the name, age, sex, and residential address of the research participant unless this information is supposed to be kept confidential by law. For confidential reports, the participant's name and street address should not be included, but the participant's age, sex, and residential zip code should be reported.

Reportable Abuse and Harm

Investigators who have reason to believe a child or elderly person is being abused may be required by Maryland law to file a report with the appropriate agency. If a participant reports current abuse, investigators likely need to file a report. Disclosures of past abuse also may need to be reported. Maryland abuse reporting guidelines can be found at the Web sites for Child Protective Services [<http://www.dhr.state.md.us/cps/report.htm>] and Adult Protective Services [<http://www.dhr.state.md.us/how/srvadult/protect.htm>]. If a participant threatens serious harm to self or other(s), investigators may need to seek hospital-based treatment for the participant, warn the intended victim(s), and/or notify police.

Investigator Responsibilities

With respect to reportable diseases and conditions, investigators must do the following:

- Determine and comply with applicable state reporting requirements.
- When conducting research internationally, determine and comply with the reporting requirements of the relevant country or locality.
- Determine and comply with confidentiality requirements. Most reporting is not confidential; in other words, the identity of the affected participant is disclosed. However, reporting of some diseases, such as HIV infection and AIDS, must occur without disclosure of a participant's identity.
- In the consent documents, (1) state the diseases and conditions that investigators are required to report that may be detected in the course of research and (2) specify whether the participant's identity will be kept confidential in the reporting.

Applicable Regulations and Guidelines

45 CFR 46

OHRP *Guidance on Certificates of Confidentiality*.

[<http://www.hhs.gov/ohrp/humansubjects/guidance/certconf.htm>]

Under section 301(d) of the Public Health Services Act [42 USC 241(d)], the Secretary of Health and Human Services may authorize persons engaged in biomedical, behavioral, clinical, or other research to protect the privacy of individuals who are participants in that research. This authority has been delegated to the National Institutes of Health.

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Section Four: Education & Training
Date of Revision: 12/13/14

Introduction

Ensuring the protection of human research participants requires that HIRB members, HIRB Office staff, and investigators understand and apply high ethical standards to the review and conduct of human participant research. Knowledge of and compliance with all relevant Federal, state, and local laws and regulations that apply to human participant research is required. To help achieve these objectives, the Homewood Human Research Protection Program (HRPP) supports a variety of educational activities on the ethical conduct and regulatory aspects of human participant research.

Educational activities supported by the Homewood HRPP include training that must be completed by HIRB members, HIRB Office staff, and all research team members working with human participants or their identifying information. Additionally, various ongoing activities are available to complement the required training. These activities are intended to help investigators recognize and resolve issues concerning research ethics and regulations that they may encounter in the planning and conduct of their research. Required training is strongly endorsed by OHRP as a component of the Homewood Schools' Federalwide Assurance (FWA).

Section Objective

The purpose of this section is to present the research training requirements for HIRB members, HIRB Office staff, investigators and others (e.g., collaborators, consultants, subcontractors, students, and staff) involved in the conduct of human participant research. In addition, ongoing educational activities that complement the required training are described.

Relevant Definitions

FEDERALWIDE ASSURANCE (FWA) A written, binding commitment submitted to OHRP by an institution engaged in human participant research in which the institution promises to comply with applicable Federal regulations governing such research and specifies the procedures it will follow to ensure compliance [45 CFR 46.103]. The Johns Hopkins University Homewood Schools' Federalwide Assurance is No. 00005834.

HRPP (HUMAN RESEARCH PROTECTIONS PROGRAM) The array of protections that are in place throughout the Homewood Divisions to ensure the rights and safety of human participants in research associated with the divisions.

IDENTIFYING INFORMATION Any item or combination of items in the data that could lead directly or indirectly to the identification of a research participant [45 CFR 46.102(f)].

OHRP (OFFICE FOR HUMAN RESEARCH PROTECTIONS) An administrative office within the Department of Health and Human Services (DHHS). OHRP implements Federal regulations for the

protection of human research participants [45 CFR 46] and provides guidance on ethical issues in biomedical and behavioral research.

4.1 HIRB Member Training

All HIRB members, including the Chair, must complete the online training program for IRB members offered by the [Collaborative Institutional Training Initiative](http://CITIprogram.org) (CITIprogram.org) within one month of their appointment to the HIRB. IRB members that are also researchers only have to complete the IRB Member training. Training expires after five years and therefore must be completed every again five years.

4.2 HIRB Staff Training

HIRB staff, including the HIRB Director, must complete the Johns Hopkins University computer-based human participant research training program, provided through the [Collaborative Institutional Training Initiative](http://CITIprogram.org) (CITIprogram.org), including both the modules for researchers and IRB members, within the first month of employment. Training expires after five years and therefore must be completed every again five years.

New and existing guidelines and regulations governing human participant research are routinely discussed at bi-weekly HIRB staff meetings. Attendance at local and regional meetings, bioethics seminars, and Federal advisory committee sessions is recommended. Participation in IRB online forums is encouraged.

4.3 Investigator Training Requirements

Except as noted below, all investigators, collaborators, consultants, subcontractors, students, staff, and other key study personnel who will be involved in a human participant research project under HIRB's jurisdiction must complete the Johns Hopkins University computer-based human participant research training program, provided through the [Collaborative Institutional Training Initiative](http://CITIprogram.org) (CITIprogram.org) prior to submission of an application for HIRB review of new research. Investigators and other research team members who join a human participant research project after it has been approved must complete the required training before involvement with participants or participants' data. These rules apply regardless of the funding source, lack of funding, or where the research is performed. Upon successful completion of the required modules, investigators can print a certificate as evidence of their training in human participant research. Training of Johns Hopkins University personnel expires after five years and therefore must be completed by all researchers every five years.

Research personnel primarily affiliated with Johns Hopkins Medicine (JHM) or the Bloomberg School of Public Health (BSPH) may meet the training requirement by completing their schools' human participant research online training course within the time frame required for that school.

Research personnel outside JHU may satisfy the training requirement by providing evidence of IRB training from their local institution prior to HIRB review. Otherwise, outside researchers must complete the Johns Hopkins University computer-based human participant research training program, provided through the [Collaborative Institutional Training Initiative](http://CITIprogram.org) (CITIprogram.org) prior to review.

Researchers transferring from another institution to JHU may, during their first six months at JHU, provide evidence of training completed while at their former institution not more than six months prior to transferring to JHU. After six months at JHU, transferred researchers must complete the Johns Hopkins University CITI module (CITIprogram.org).

4.4 Outreach Activities

HRPP supports a variety of activities and resources intended to compliment the required training in human participant research.

HIRB Newsletter

Periodically HIRB releases a newsletter containing pertinent information on the planning, review, and conduct of human participant research. The newsletter is posted on the HIRB Web site.

Brown Bag Sessions

During the academic year, the HIRB Office may organize brown bag sessions that focus on ethical and regulatory issues related to the planning, review, and conduct of human participant research. The sessions are open to all faculty, students, staff, and guests.

Educational Materials and Guidelines

Investigators have access to the HIRB Investigator's Manual and Standard Operating Policies and Procedures, the latter of which lists resources and references on key topics. Both documents are continuously updated and available on the HIRB Web site.

Members of HIRB receive an IRB Members Handbook, which describes the principal functions of the IRB and their roles as members, the HIRB Reviewer's Guide, and a complete and continuously updated set of HIRB Standard Operating Policies and Procedures to use as resources when reviewing proposed research protocols and progress reports. In addition, the HIRB Director schedules educational sessions during HIRB meetings. Members also receive educational pamphlets, regulatory guidelines, and announcements relevant to human participant research. Copies of the *Human Research Report* and access to an online IRB forum are available in the HIRB Office.

Consultation with HIRB Office Staff

HIRB Office staff members are available daily to meet with faculty, staff, and students to discuss issues related to the planning and review of their research.

Local, Regional, and National Meetings and Courses

The Homewood Divisions provide support for HRPP members and HIRB members and staff to attend local and regional meetings and take part in courses and workshops that focus on issues related to the ethical and regulatory conduct of human participant research.

Applicable Regulations & Guidelines

OHRP (January 6, 2005). *Federalwide Assurance (FWA) for the Protection of Human Subjects*.
[<http://www.hhs.gov/ohrp/humansubjects/assurance/filasurt.htm>]

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Section Five: Review Procedures: Applications for New Research
Date of Revision: 12/16/14

Introduction

The Homewood Institutional Review Board (HIRB) is responsible for reviewing all human participant research under its jurisdiction, in accordance with the JHU Homewood Schools' Federalwide Assurance (FWA). Homewood researchers must first determine, with assistance from HIRB Office staff when needed, whether their research will involve human research participants. If so, they must complete and submit to HIRB an Application for Exemption or an Application for Expedited/Full Board Review. HIRB review of new research is one of HIRB's primary responsibilities and protects participants' rights and well-being by assuring research project compliance with Federal, state, and local laws and regulations and HIRB policies and procedures. Contact with human participants and identifiable private information is not permitted until HIRB has exempted or approved human participant research. Collaborating institutions, including external performance sites (i.e., places outside the Homewood Schools where some or all of the research will take place), may also require IRB approval, depending upon whether the collaborating institution qualifies as engaged in research.

Section Objective

The purpose of this section is to specify what constitutes human participant research and distinguish when institutions are engaged in research. In addition, the application process for HIRB review of new research is described. HIRB reviews research at three different levels: exempt, expedited, and full board. Review at each of these levels is detailed.

Relevant Definitions

ENGAGED IN RESEARCH An institution becomes engaged in human participant research when its employees or agents (i.e., individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility) intervene or interact with living individuals for research purposes or obtain individually identifiable private information for research purposes [45 CFR 46.102(d & f)].

EXEMPT REVIEW Review to determine if a study is minimal risk and falls into one of six categories delineated in Federal regulations as potentially exempt. [45 CFR 46.101] Studies deemed exempt by HIRB are released from compliance with Federal regulations [45 CFR 46] at HIRB's discretion. Investigators are nevertheless required to treat participants ethically.

EXPEDITED REVIEW Review of proposed human participant research by the HIRB chair or one or more designated voting members instead of the full board. Federal rules permit expedited review for certain categories of research involving no more than minimal risk and for minor changes in ongoing research the IRB has previously approved [45 CFR 46.110].

FEDERALWIDE ASSURANCE (FWA) A written, binding commitment submitted to OHRP by an institution engaged in human participant research in which the institution promises to comply with applicable Federal regulations governing such research and specifies the procedures it will follow to ensure compliance [45 CFR 46.103]. The Johns Hopkins University Homewood Schools' Federalwide Assurance is No. 00005834.

FULL BOARD REVIEW Review of a proposed human participant research project at a convened IRB meeting at which a majority of members is present, including at least one member whose primary concerns are not scientific. A majority of those present must approve the research for it to receive IRB approval [45 CFR 46.108].

IDENTIFYING INFORMATION Any item or combination of items in the data that could lead directly or indirectly to the identification of a research participant [45 CFR 46.102(f)].

HUMAN PARTICIPANT RESEARCH When an investigator obtains, for research purposes, (1) data through intervention or interaction with a living individual or (2) identifiable private information about a living individual.

OHRP (OFFICE FOR HUMAN RESEARCH PROTECTIONS) An administrative office within the Department of Health and Human Services (DHHS). OHRP implements Federal regulations for the protection of human research participants [45 CFR 46] and provides guidance on ethical issues in biomedical and behavioral research.

PRIVATE INFORMATION Includes facts about attitudes and behaviors that an individual can reasonably expect not to be shared with people the individual has not authorized to have access to the information [45 CFR 46.102(f)]. Examples include medical records, school records, and answers to survey questions about illegal and embarrassing behaviors.

PROTOCOL The formal design or plan of an experiment or research activity which is submitted to an IRB for review and often also used in applications to funding agencies. The protocol includes a description of the proposed research design and methodology, eligibility requirements for prospective participants, informed consent process, treatment regimen(s), and methods of analysis that will be performed on the data collected. The body of HIRB applications for new research consists of the research protocol.

RESEARCH A systematic investigation designed to develop or contribute to generalizable knowledge. May include research development, testing, and evaluation activities [45 CFR 46.102].

5.1 What Constitutes Human Participant Research and Is Subject to HIRB Review

HIRB must exempt or approve human participant research within its jurisdiction before contact with participants or identifiable private information is initiated. The following questions should be answered sequentially to determine whether an activity (excluding class projects and independent student research) is human participant research and, thus, requires exemption or approval by HIRB. (Also see Chart 1 in Appendix A.)

Note: Special considerations apply to class projects and student research. See Class Projects in Section 7.1 and Individual Student Research Projects in Section 7.2 for details.

1. Does the proposed activity meet the definition of research?

- Research is a systematic investigation that is designed to develop or contribute to generalizable knowledge and may include research development, testing, and evaluation. Activities that meet this definition constitute research for purposes of HIRB policy, regardless of whether they are conducted or supported under a program that is considered research for other purposes.
 - If an activity does not meet this definition of research and is not a class project or individual student research, HIRB review and approval are not required.
2. Does the study constitute human participant research?
- Human participant research is research that involves a living individual about whom an investigator (whether faculty member, staff member, or student) 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 (e.g., venipuncture) and manipulations of the participant or the participant's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and participant.
 - Private information includes (1) information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place and (2) information disclosed for specific purposes by an individual which the individual can reasonably expect will not be made public (e.g., school and medical records). Private information must be individually identifiable (i.e., the identity of the participant is or may readily be ascertained by the investigator or associated with the information) in order for the collection of information to constitute human participant research.
 - Since the regulations define a human research participant as a living individual, research involving the deceased is not human participant research and does not require review and approval by HIRB.
 - HIRB must review and either exempt or approve all research under its jurisdiction that meets the definition of human participant research.
3. Will the Homewood Schools be engaged in human participant research?
- When Homewood employees or agents (i.e., individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility) intervene or interact with living individuals or obtain, release, or access identifiable private information about living individuals for research purposes, the Homewood Schools are engaged in human participant research, even when the research is conducted at and/or led by a PI from another institution, according to Federal regulations [45 CFR 46.102]. Similarly, when any of the Homewood Schools receives a direct DHHS award to support human participant research, the Homewood Schools are engaged in research and bear ultimate responsibility for protecting human participants under the award, even if a subcontractor or collaborator carries out all of the research activities.

- When the Homewood Schools will be engaged in human participant research, that research must be reviewed and approved by HIRB, unless HIRB has officially delegated review to the IRB of a collaborating institution.

In summary, the Homewood Divisions are engaged in research that must be reviewed by HIRB, unless HIRB has officially delegated review to the IRB of a collaborating institution, if *any* one of the following is true:

- Homewood employees, students, or agents intervene or interact with living individuals for research purposes.
- Homewood employees, students, or agents obtain individually identifiable private information for research purposes.
- A Homewood School receives a direct DHHS award to support human participant research.

Investigators are encouraged to contact the HIRB Office for assistance in determining whether a proposed activity is human participant research that requires review and either exemption or approval by HIRB whenever they have any doubt. Final determinations as to whether an activity is human participant research and whether an institution is engaged in research lie with HIRB and are made on a case-by-case basis.

5.2 Institutions Engaged in Research

As detailed in the previous section, when Homewood employees or agents (i.e., individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility) intervene or interact with living individuals or obtain, release, or access identifiable private information about living individuals for research purposes, the Homewood Schools are engaged in human participant research, even when the research is conducted at and/or led by a PI from another institution, according to Federal regulations. Similarly, when any of the Homewood Schools receives a direct DHHS award to support human participant research, the Homewood Schools are engaged in research and bear ultimate responsibility for protecting human participants under the award, even if a subcontractor or collaborator carries out all of the research activities. When the Homewood Schools will be engaged in human participant research, that research must be reviewed and approved by HIRB, unless HIRB has officially delegated review to another IRB.

Furthermore, when Homewood faculty, staff, or students plan to collaborate on human participant research with another institution that qualifies as engaged in research with respect to the study, HIRB must receive evidence of IRB approval from the collaborating institution, as well as the Federalwide Assurance (FWA) number of the collaborating institution if the study is Federally-funded, before HIRB approves the study. IRB approval from the collaborating institution pending HIRB approval is allowed. (See Section 1.4 for options if the collaborating institution does not have its own IRB.) Collaborating institutions are not limited to other universities or organizations frequently involved in research; they may include external performance sites where the research takes place (e.g., elementary schools, homeless shelters, clinics, and nursing homes). If the collaborating institution is not engaged in research, IRB approval from the collaborating institution is not needed.

It is not always easy to determine when an institution is engaged in research. Examples to differentiate activities that constitute engagement in research from nonengagement are provided

below. Investigators are encouraged to contact the HIRB Office for further assistance in determining whether an institution is engaged in research.

Engaged in Research Examples

An institution is considered engaged in research with respect to a specific study if the research is nonexempt, involves human research participants, and the institution's involvement fits into any of the eight categories listed below.

1. The institution's employees or agents intervene directly with living individuals by performing invasive or noninvasive procedures for research purposes. An intervention includes both physical procedures (e.g., blood drawing) and manipulation of the participant for research purposes (e.g., use of behavior modification). Examples:
 - Rewarding individuals participating in a study for performing certain behaviors; collecting biological samples; giving drugs or other treatments; using medical technologies; using physical sensors.
2. The institution's employees or agents intervene indirectly with living individuals by manipulating the environment for research purposes. Examples:
 - Orchestrating environmental events or social interactions; controlling environmental light, sound or temperature; presenting sensory stimuli; making voice, digital, or image recordings.
3. The institution's employees or agents interact with living individuals for research purposes. Examples:
 - Engaging in protocol-dictated communication or interpersonal contact; conducting research interviews; obtaining informed consent. (See Not Engaged in Research #3 below for description of interactions that do not constitute engagement in research.)
4. The institution's employees or agents release individually identifiable information or permit investigators to obtain individually identifiable information, without the participants' explicit written permission. Examples:
 - Releasing patients' names to investigators for solicitation as research participants; permitting investigators to record private information from school, employment, or medical records in individually identifiable form. (See Not Engaged in Research #5 below regarding release of such information with participants' prior written permission and #6 regarding release of such information to a state or local health department.)
5. The institution's employees or agents obtain, receive, or possess private information that is individually identifiable (either directly or indirectly through coding systems) for research purposes. Examples:
 - Obtaining private information from school or medical records in an individually identifiable form. (See Not Engaged in Research #7 and #8 below for activities that involve release of information and/or specimens in nonidentifiable form.)

6. The institution's employees or agents obtain, receive, or possess private information that is individually identifiable (directly or indirectly through coding systems) for the purpose of maintaining a statistical center for multi-site collaborative research. Where institutional activities involve no interaction or intervention with participants and the principal risk associated with institutional activities is limited to the potential harm resulting from a breach of confidentiality, the IRB does not need to review each collaborative protocol. However, the IRB should determine and document that the statistical center has sufficient mechanisms in place to ensure that (a) the privacy of participants and the confidentiality of data are adequately maintained, given the sensitivity of the data involved; (b) each collaborating institution holds an applicable OHRP-approved FWA; (c) each protocol is reviewed and approved by an IRB at the collaborating institution prior to the enrollment of participants; and (d) informed consent is obtained from each participant in compliance with Federal regulations.
7. The institution's employees or agents maintain a coordinating center for multi-site collaborative research. Where institutional activities involve no interaction or intervention with participants, the IRB need not review each collaborative protocol. However, the IRB should determine and document that the coordinating center has sufficient mechanisms in place to ensure that (a) management, data analysis, and data safety and monitoring systems are adequate, given the nature of the research involved; (b) sample protocols and informed consent documents are developed and distributed to each collaborating institution; (c) each collaborating institution holds an applicable OHRP-approved FWA; (d) each protocol is reviewed and approved by an IRB at the collaborating institution prior to the enrollment of participants; (e) any substantive modification by a collaborating institution of sample consent information that is related to risks or alternative procedures is appropriately justified; and (f) informed consent is obtained from each participant in compliance with Federal regulations.
8. The institution receives a direct DHHS award to conduct the research, even when a subcontractor or collaborator carries out all activities involving human participants.
Example:
 - A collaborating institution receives a DHHS award for a study and contracts with JHU to conduct all research-related activities and vice versa.

Not Engaged in Research Examples

An institution is not engaged in human participant research with respect to a specific study if its involvement is limited to the following:

1. The institution's employees or agents act as consultants on the research but at no time obtain, receive, or possess identifiable private information. Example:
 - A consultant analyzes data that cannot be linked to individual participants, either directly or indirectly through coding systems, by any member of the research team.
 - Should a consultant access or utilize individually identifiable private information while visiting the research team's institution, the consultant's activities become subject to the oversight of the research team's IRB. However, the consultant's institution is *not* considered to be *engaged* in the research and would not need an FWA or IRB approval.

- Should a consultant obtain coded data for analysis at the consultant's institution, the consultant's institution *is* considered *engaged* in human participant research and would need an FWA and IRB approval, unless a written agreement unequivocally prohibits release of identifying codes to the consultant. Example:
 - The consultant analyzes coded data, but a written agreement prohibits everyone at the consultant's institution, including the consultant, from access to information linking the codes to individual participants.
2. The institution's employees or agents (a) perform commercial services for the investigators or perform other genuinely noncollaborative services meriting neither professional recognition nor publication privileges and (b) adhere to commonly recognized professional standards for maintaining privacy and confidentiality. Examples:
 - A qualified individual or agency conducts prespecified statistical analyses of nonidentifiable data for payment. An appropriately qualified laboratory analyzes blood samples for investigators solely on a commercial basis.
 3. The institution's employees or agents (a) inform prospective research participants about the availability of research; (b) provide prospective research participants with written information about research, which may include a copy of the relevant informed consent document and other IRB-approved materials, but do not obtain participants' consent or act as authoritative representatives of the investigators; (c) provide prospective participants with information about contacting investigators for information or enrollment; or (d) obtain and appropriately document prospective participants' permission for investigators to contact them. Examples:
 - An employee gives potential participants literature about a research study, including a copy of the informed consent document, and tells them how to contact the investigator if they want to enroll. An employee gives investigators contact information about potential participants after receiving explicit permission from each potential participant to be contacted.
 4. The institution (e.g., a school, nursing home, or business) permits use of its facilities for intervention or interaction with participants by research investigators. Examples:
 - A school permits investigators to test students whose parents have provided written permission for their children to participate. A business permits investigators to solicit research volunteers at its work site.
 5. The institution's employees or agents release identifiable private information to investigators with the prior written permission of participants. Example:
 - With the written permission of participants, a clinician releases the participants' medical records to investigators.
 6. The institution's employees or agents release identifiable private information or specimens to a state or local health department or its agent for legitimate public health purposes within the recognized authority of that department. (However, utilization of such information or

specimens by department investigators for research purposes would constitute engagement in research and would require an FWA and IRB approval.)

7. The institution's employees or agents release information or specimens to investigators in nonidentifiable (i.e., nonlinkable) form, where the institution has obtained such information or specimens for purposes other than the investigators' research. Examples:
 - A school releases to investigators aggregate demographic data about its students; the data contain no identifying information and no codes or other linkages to identifying information. Nursing home employees provide investigators with a data set containing medical record information, but the data set contains no direct or indirect identifiers through which the identity of individual participants could be ascertained, either by the investigators or by nursing home personnel. A hospital pathology department releases excess tissue specimens and relevant medical record information to investigators, but these materials include no direct or indirect identifiers through which the identity of individual participants could be ascertained, either by investigators or by hospital personnel, including those in the pathology department.
8. The institution's employees or agents receive information or specimens from established repositories operating in accordance with (a) an applicable OHRP-approved FWA, (b) OHRP guidance, and (c) written agreements that unequivocally prohibit release of identifying information to recipient investigators.

Note: These activities may be certified as exempt by HIRB. See Section 5.6, Exempt Category #4.

9. The institution's clinical staff provides protocol-related care or follow-up to participants enrolled at distant sites by clinical trial investigators in an OHRP-recognized Cooperative Protocol Research Program (CPRP). In such cases, the CPRP clinical trial investigator (consistent with a registered investigator as defined in Section 14.1 of the NCI Investigator's Handbook) retains responsibility for oversight of protocol related activities; clinical staff may not accrue participants or obtain informed consent for research participation; clinical staff may only provide data to the investigator in accordance with the terms of informed consent; and the informed consent document should state that such data are to be provided by clinical staff as directed by the investigator.

5.3 When Homewood Personnel Assist a Non-JHU PI

Occasionally Homewood personnel will assist a non-JHU PI with research involving human participants. For instance, Homewood personnel may serve as consultants, recruit participants, or collect data, among other activities, for a non-JHU PI. When the activities of Homewood personnel constitute research and thereby qualify the Homewood Schools as engaged in research, Homewood personnel must obtain HIRB approval of the study. This is a Federal requirement. Homewood personnel cannot engage in human participant research without prior HIRB approval. If the activities of Homewood personnel do not qualify the institution as engaged in research, HIRB approval of the study is not needed. HIRB Office staff members are available to discuss this requirement when needed.

The non-JHU PI generally will apply to his or her own institution for IRB approval of the study and is not required to apply directly to HIRB. However, as stated above, when the collaboration of Homewood personnel qualifies the Homewood Schools as engaged in research, Homewood

personnel must obtain HIRB approval. In most cases, the non-JHU PI's IRB also will require evidence of HIRB approval. The non-JHU PI's assistance to Homewood personnel in the preparation of an application for HIRB approval of the study likely will be indispensable.

5.4 HIRB Review Levels

HIRB reviews research at three levels: exempt, expedited, and full board. All applications for new research projects that involve human participants must be reviewed and either exempted or approved by HIRB before contact with human research participants or their identifiable data may begin. Similarly, HIRB must review and reapprove all ongoing nonexempt research at least annually, as well as review and approve all requests to amend the research protocol or consent documents before any changes are implemented.

The type of review required depends in part upon the level of risk involved. Certain studies that involve no greater than minimal risk may qualify as exempt from Federal regulations or be reviewed at the expedited level. According to OHRP, a study is minimal risk if “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.” An exempt classification is given only to minimal risk research that fits into one or more of six Federally-approved exemption categories, which are listed in Section 5.6. An expedited review can be conducted on minimal risk research that falls within one or more expedited review categories, which are listed in Section 5.7. Investigators may apply for exemption or request expedited review; however, HIRB has final responsibility for determining the type of review needed. All projects that involve greater than minimal risk are reviewed by the full board at a convened meeting attended by a majority of the voting members, including a nonscientist.

5.5 Application Procedures for New Studies

New applications for research must be submitted through the eHIRB online submission system (<https://ehirb.jhu.edu/ehirb/>). Federal regulations lay out specific criteria for IRB review and approval of new and continuing human participant research. To assist researchers and facilitate the review process, HIRB has developed materials for the preparation and submission of research applications, including forms, instructions, and checklists to ensure that applications contain all of the information and documentation required for review.

Instructions for preparing and submitting applications for new research studies should be followed carefully. Required checklists should be completed, and required documentation should be provided. All applications must contain the signature of the PI or be submitted from the PI's email address. In the case of student-initiated projects, the PI must complete and sign the “Supervisor Responsibilities” form. Incomplete submissions will be returned to the PI, and the review process will not commence until a complete application is received. Researchers who have questions concerning any aspect of the application and review process are strongly encouraged to discuss them with HIRB Office staff early in the preparation process. Investigators who believe their research project qualifies for exemption from Federal regulations should complete and submit the HIRB Application for Exemption, in which they present their research protocol.

Common Application Mistakes

HIRB reviews all components of submitted applications for approval of new research, including the research protocol (which is contained within the application), informed consent documents, supporting documents, and funded or high scoring grant or contract proposals. Investigators should carefully, thoroughly, and consistently prepare each component. The research protocol and supporting documents should contain sufficient detail for HIRB to assess whether protections for human research participants are adequate. Investigators are advised to comply with the following in order to avoid common mistakes:

- The main body of the application consists of the research protocol. Although consent forms and supporting documents are submitted within the application, it is not acceptable to refer reviewers to these documents for information requested in the research protocol, unless the directions specify that the information should be placed in an attached document.
- The research protocol should be written in nontechnical language so that all HIRB members, including the nonscientist, can comprehend it.
- Every application item should be fully and accurately completed. Incomplete protocols will be returned to the PI for completion, delaying the review process.
- Responses to open-ended items should be detailed, and investigators should provide the rationale for their procedures to facilitate HIRB's evaluation of their adequacy and acceptability.
- The information in the research protocol must match the information in the consent documents.
- If a waiver or alteration of informed consent is requested, the request must be justified.
- The information in the research protocol should not conflict with the information in grant or contract proposals. Discrepancies could delay the review process and, if unavoidable, should be explained.
- If women, racial or ethnic minorities, or children are excluded from the study, these exclusions should be thoroughly justified.
- If research is being conducted in an off-campus location, permission from that site will likely be required for IRB review.

When and Where to Submit Applications for New Studies

Applications for exempt research should be submitted through eHIRB (<https://ehirb.jhu.edu/ehirb/>) at least 30 days before the research is expected to begin.

Applications for nonexempt research should be submitted through eHIRB (<https://ehirb.jhu.edu/ehirb/>) at least 60 days before the research is expected to begin.

Grant and contract proposals to fund human participant research typically do not require HIRB approval before they are submitted to funding agencies for review. Federal regulations require, however, that HIRB exempt or approve all proposals that involve human participant research. Funds awarded by the sponsors will not be released by JHU, or the funders themselves in some cases, until HIRB has reviewed and approved the grant or contract proposal along with the research

protocol. To avoid a delay in funding, investigators who are notified that their proposal or contract will be funded or that a proposal has received a score that appears to be in a fundable range should submit their application and proposal promptly to HIRB for review.

5.6 HIRB Review — Exempt

As specified in Federal regulations, six categories of minimal risk research are potentially exempt from the Federal Policy for the Protection of Human Subjects [45 CFR 46.101]. Investigators must apply for exemption, and HIRB has the authority to exempt qualifying research from Federal regulations. The HIRB Director reviews each Application for Exemption to determine if the study meets the criteria for exemption set forth in the Federal regulations, such as no more than minimal risk and research activities that fall entirely within the exemption categories. Research involving any of the following is not eligible for exemption: children who will be surveyed or interviewed; prisoners; pregnant women, fetuses, or neonates; and deception. (See Chart 2 in Appendix A.)

Investigators whose research qualifies as exempt are still obligated to treat participants ethically, which typically includes informing potential participants of their rights and obtaining their consent, oral or written, to participate. HIRB requires that investigators applying for exemption describe and justify their consent process or the lack thereof. Consent documents (e.g., disclosure statements, scripts for oral consent, abbreviated written consent documents, regular written consent documents), if any, should be submitted as part of the application. Investigators are also expected to notify the HIRB when all data analysis has been completed on an exempt study so that the HIRB can update their files.

Exempt Categories

The following categories of research may qualify for exemption:

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (a) research on regular or special education instructional strategies or (b) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods [45 CFR 46.101(b)(1)]. (See Chart 3 in Appendix A.)
2. Research involving the use of educational tests (e.g., cognitive, diagnostic, aptitude, and achievement tests), survey procedures, interview procedures, or observation of public behavior, unless: (a) information obtained is recorded in such a manner that the human research participant can be identified, directly or through identifiers linked to the participant and (b) any disclosure of the human participant's responses outside the research context could reasonably place the participant at risk of criminal or civil liability or be damaging to the participant's financial standing, employability, or reputation [45 CFR 46.101(b)(2)]. (See Chart 4 in Appendix A.)

Note: Observations of public behavior that include children can qualify as exempt research only if the investigator does not participate in the activities being observed. Research utilizing surveys or interview procedures that includes children cannot qualify as exempt research.

3. Research involving the use of educational tests (e.g., cognitive, diagnostic, aptitude, and achievement tests), survey procedures, interview procedures, or observation of public behavior that is not exempt under category (2) above, if: (a) the human participants 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 [45 CFR 46.101(b)(3)]. (See Chart 4 in Appendix A.)

4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if the sources are publicly available [45 CFR 46.101(b)(4)]. (See Chart 5 in Appendix A.)

Note: This item concerns publicly available data that contain identifiers or can be linked to specific individuals. EXISTING means that the data, documents, records, or specimens were collected prior to submission of the Application for Exemption.

Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if the information, although initially containing identifiers, is recorded by the investigator in such a manner that participants cannot be identified, directly or through identifiers linked to the participants [45 CFR 46.101(b)(4)]. (See Chart 5 in Appendix A.)

Note: This item concerns research on existing data, whether publicly available or not, that have been recorded by the investigator in a manner that does not allow individual participants to be identified or links to individual participants to be reestablished. If any person can link these data, documents, records, or specimens to specific individuals, the research does not qualify as exempt. Research on existing data, whether publicly available or not, that do not contain identifiers and cannot be linked to personal identifiers is not human participant research and does not require review by HIRB.

5. Research and demonstration projects that are conducted by or subject to the approval of 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 payments for benefits or services under those programs [45 CFR 46.101(b)(5)]. (See Chart 6 in Appendix A.)

Note: According to OHRP, this category generally applies only to Social Security benefit programs, procedures for obtaining benefits under these programs, or possible changes in these programs.

6. Taste and food quality evaluation and consumer acceptance studies, if (a) wholesome foods without additives are consumed or (b) a food is consumed that contains a food ingredient at or below the level and for a use found to be safe or an 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 [45 CFR 46.101(b)(6)]. (See Chart 7 in Appendix A.)

HIRB requires status reports every three years for exempt research. The PI must notify HIRB of any changes in the research plan that might affect HIRB's initial determination of exempt status.

5.7 HIRB Review — Expedited

Federal regulations allow for certain categories of research presenting no greater than minimal risk to be reviewed through an expedited review process. Expedited review does not guarantee that the review will occur more quickly than full board review.

If any part of the proposed research is more than minimal risk, it must be reviewed by the full board. Research is not eligible for expedited review if the identification of participants or their responses will place them at risk of criminal or civil liability or be damaging to their financial standing, employability, insurability, or reputation, unless reasonable and appropriate protections will be implemented so that these risks are not greater than minimal. Classified research is also not eligible for expedited review. (See Chart 8 in Appendix A.) The HIRB Chair and Director determine whether studies qualify for expedited review. The HIRB Chair can send studies that fit within the expedited review categories to the full board at his or her discretion.

Research that qualifies for expedited review is reviewed by one or more HIRB members or the Chair. The Chair has designated the duty to conduct expedited reviews to any of the trained IRB members. The expedited reviewer(s) receive the application, consent documents, and other materials, such as questionnaires, advertisements and recruitment letters. Expedited reviewers may approve a research project or request revisions but may not disapprove it. To approve, the expedited reviewers determine whether the project and proposed study methods meet the criteria for approval. The consent document is reviewed for accuracy, clarity, and inclusion of required and optional elements. If the expedited reviewer(s) are unable to approve a project even after requesting and receiving revisions from the PI, the study is forwarded to the full board for review.

All research approved under an expedited review procedure is reviewed again at least annually.

A summary of all research approved through the expedited procedure is distributed to HIRB members on a monthly basis.

Expedited Categories

The categories of research eligible for expedited review are listed below. Research can qualify for expedited review regardless of whether the participants include children, except as noted below. Categories 1-7 apply to both review of new research and continuing review, while items 8 and 9 refer only to continuing 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 (IND) application is not required [21 CFR Part 812]. (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 (IDE) application is not required [21 CFR 812] or (ii) the medical device is cleared/approved for marketing and the medical device will be used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture under condition (a) or (b):

- a. From healthy, nonpregnant adults, who weigh at least 110 pounds. (Amounts drawn may not exceed 550 ml in an eight week period and collection may not occur more than two times per week.)
 - b. From other adults and children, considering the age, weight, and health of the participants, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. (The amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an eight week period, and collection may not occur more frequently than two times per week.)
- Prospective collection of biological specimens for research purposes by noninvasive means. Examples:
 - c. Hair and nail clippings, in a nondisfiguring manner.
 - d. Deciduous teeth at the time of exfoliation or if routine patient care indicates a need for extraction.
 - e. Permanent teeth if routine patient care indicates a need for extraction.
 - f. Excreta and external secretions, including sweat.
 - g. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or applying a dilute citric solution to the tongue.
 - h. Placenta removed at delivery.
 - i. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor.
 - j. 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.
 - k. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings.
 - l. Sputum collected after saline mist nebulization.
- 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:
 - m. 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 participant or an invasion of the participant's privacy.
 - n. Weighing or testing sensory acuity.
 - o. Magnetic resonance imaging.

- p. Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography.
- q. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
- Research involving materials (data, documents, records, or specimens) that have been or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).
- Collection of data from voice, video, digital, or image recordings made for research purposes.
- 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.
- Continuing review of research previously approved by the convened IRB when *any* one of the following applies:
 - r. The research is permanently closed to the enrollment of new participants, all participants have completed all research-related interventions, AND the research remains active only for long-term follow-up of participants.
 - s. No participants have been enrolled, and no additional risks have been identified.
 - t. The remaining research activities are limited to data analysis.
- 9. Continuing review of research, not conducted under an IND application or IDE, where categories 2–8 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.

5.8 HIRB Review — Full Board

Human participant research that does not qualify for exemption or expedited review must be reviewed at a HIRB full committee meeting. In order to review the research, a majority of the voting members must be present, including at least one member whose primary concerns are nonscientific. A physician must be present when reviewing FDA-regulated research. The board cannot review research if a quorum (i.e., a majority of current HIRB members, including a nonscientist) fails during the meeting due to recusal of members with conflicting interests, early departure of members, absence of a nonscientist, or other legitimate reasons. A full board meeting may be cancelled for lack of a quorum or other reasons cited by the Chair.

Applications are placed on the board's agenda in the order in which they are received in the HIRB Office. The schedule of full board meetings is available on the HIRB Web site. The HIRB Director

or Chair assigns each application to a primary reviewer. When possible, the primary reviewer is the board member with the most expertise in the area of the study.

Application materials are sent to HIRB members at least one week before the full board meeting. Those attending the meeting receive the application, consent documents (forms and/or scripts), and recruitment materials, such as advertisements and recruitment letters. The primary reviewer also receives the following documents if applicable: the complete grant or contract proposal, sponsor's protocol, questionnaires, and Investigator's Brochure in studies of investigational devices.

During the review, the primary reviewer summarizes his or her review of the project and states his or her recommendations. At the discretion of the Chair, the investigator may be invited to attend the meeting to clarify unresolved issues. The investigator must, however, leave during the discussion and not be present for the vote. The board determines whether the project and proposed study methods meet the criteria for approval (see Section 5.9). The consent document is reviewed for accuracy, clarity, and inclusion of required and optional elements. By a majority of board members present at the meeting, a project is either: (1) approved as submitted, (2) approved pending receipt of minor revisions, (3) deferred until a revised application can be reviewed at a subsequent full board meeting, or (4) disapproved. When specific minor changes are requested by the board as a condition for approval and only the PI's acceptance of the requested changes is required for approval, the board will delegate review and final approval of the revisions to the Chair or a single HIRB reviewer under an expedited review procedure.

The written minutes of each full board meeting document the following: (1) attendance; (2) vote tallies, including the number of votes for, votes against, and abstentions; (3) requested changes and the basis for them; (4) reasons for disapproving any research; and (5) a summary of controverted issues and their resolution.

5.9 Criteria for Approval of New Studies

In order for HIRB to approve an Application for Expedited or Full Board Review, the research protocol and supporting documents must satisfy each of the requirements below, according to Federal regulations. [45 CFR 46.111]

1. Risks to participants are minimized by using procedures that are consistent with sound research design that do not unnecessarily expose participants to risk and, whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.
 - Risks to participants are reasonable in relation to (a) the anticipated benefits to participants (if any) and (b) the importance of the knowledge that may be reasonably expected from the study. In evaluating risks and benefits, HIRB considers only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies participants would receive even if not participating in the research). HIRB does not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy).
 - Selection of participants is equitable. In making this assessment, HIRB considers the purposes of the research and the setting in which the research will be conducted and is particularly concerned about the fairness of research involving vulnerable populations,

such as children, prisoners, pregnant women, mentally disabled persons, and economically and educationally disadvantaged individuals.

- Informed consent is sought from each prospective participant or a legally authorized representative (LAR), in accordance with and to the extent required by Federal regulations.
- Informed consent is appropriately documented, in accordance with and to the extent required by Federal regulations.
- When appropriate, the research protocol includes adequate provisions for monitoring the data collected to ensure participants' safety.
- When appropriate, the research protocol contains adequate provisions to protect the privacy of participants and to maintain the confidentiality of data.
- When some or all participants are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these participants (e.g., children, prisoners, pregnant women, mentally disabled persons, and economically and educationally disadvantaged individuals).

5.10 HIRB Determinations and Motions

Investigators may not engage in human participant research (i.e., initiate contact with potential participants or their individually identifiable data) until HIRB has exempted or approved the research project.

Exempt Review

If the HIRB Director determines a study to be exempt, a letter is sent to the PI notifying her or him that the study is exempt from Federal regulations for the protection of human research participants. The letter specifies the applicable exemption category or categories. Copies of these letters are filed in the HIRB Office. When the research is funded, copies are sent to the Assistant Provost in the JHU Research Projects Administration Office. The letter explains that further communication with HIRB is not required unless changes to the project are considered that could alter the exemption status. If the HIRB Director or Chair determines that the study does not qualify as exempt, the HIRB Director or staff will contact the PI and instruct her or him that the study must be reviewed by HIRB at the expedited or full board review level.

Expedited and Full Board Review

After reviewing Applications for Expedited or Full Board Review, HIRB renders the following determinations and motions as described below:

- ***Approved.*** A study is approved if the research activities meet the criteria for approval as defined in 45 CFR 46.111 and no changes to the research application, including supporting documents, are necessary.
- ***Approved Pending Revisions.*** An approved pending revisions decision is made when the research activity meets the criteria for approval as defined in 45 CFR 46.111 and only minor revisions are needed that require concurrence by the investigator. The PI must provide a memorandum responding to HIRB's request for modifications and submit all

modified documents with the respective changes highlighted. The application is then approved if, on subsequent review by the Chair or a designated board member, she or he finds that the investigator has satisfactorily made the revisions. For studies approved by the full board pending minor revisions, the approval date is the date of the full board meeting regardless of the duration of the revision and acceptance process.

- ***Deferred.*** A study is deferred if substantial revisions are needed to the research application or HIRB has insufficient information to render a decision. The PI must provide a memorandum responding to HIRB's concerns, comments, recommendations, and questions and submit all modified documents with the changes highlighted. If reviewed at the expedited level, the application will be reconsidered once the reviewer(s) have received the revised application. If reviewed by the full board, the application will be reconsidered at the board meeting following its resubmission.
- ***Disapproved.*** A study is disapproved if it has major scientific or ethical problems that in HIRB's judgment cannot be adequately resolved by the PI. When an application is disapproved by HIRB, the investigator(s) are not authorized to initiate the study. Applications cannot be disapproved at the expedited level; instead, they are forwarded to the full board for review.

Investigators are notified of the above determinations and motions through letters sent from the eHIRB system. Approval letters specify the expiration date for HIRB approval, a recommendation that Applications for Continuing Review should be submitted six weeks prior to the approval expiration date, a statement that changes cannot be implemented without HIRB approval, and a reminder that investigators must report unanticipated problems to HIRB. When the research is funded, copies also are sent to JHU Research Projects Administration Office.

5.11 Application Revisions

A common outcome of exempt, expedited, or full board review is a request that the research proposal or supporting documents, especially consent forms, be revised. The PI must respond satisfactorily to all requests for revisions or clarifications before the proposal can be approved by HIRB. The goal of HIRB is to work with investigators to ensure that human research participants are appropriately protected so that research projects ultimately can be approved.

If a study is classified as exempt or is under expedited review, the PI should respond directly to written questions and revise the application. When the reviewer is satisfied with the revised application and the PI's responses, he or she will exempt or approve the study and decide when the continuing review is due. If the HIRB Director is still not able to exempt the research and the Chair agrees, the PI will be notified that the study needs to undergo expedited or full board review. If the expedited reviewer is still not satisfied, the application, together with the reviewer's comments, will be sent to the full board for review.

If the initial application is reviewed by the full board, the investigator will receive a letter summarizing the board's questions and requested revisions. If the requested changes are minor and the only requirement is that the investigator agrees to the requested changes, the board may delegate review and final approval of the changes to the Chair or a single HIRB member under an expedited review procedure. If the appointed reviewer is not satisfied with the PI's response, the application, together with the reviewer's comments, will be reviewed by the full board. If the full board requires

revisions that are more than minor, the revised proposal must be reviewed by the full board at a regularly convened HIRB meeting.

5.12 Appeal of HIRB Decisions

When HIRB requires modifications to or disapproves a research protocol, it will provide justification for its determination to the PI in writing. The PI may appeal the decision to HIRB in a written letter or by written request for an appearance before the board. HIRB will consider the PI's response in rendering its final decision.

After an application has been disapproved, the PI can submit a new application and should respond to HIRB's concerns regarding the previous submission in the new application. Multiple resubmissions are allowed. HIRB will work with investigators to assist them in modifying their research so that approval can be granted.

Other JHU officials or bodies cannot approve research that HIRB has disapproved. There is no appeal process beyond HIRB, in keeping with Federal policy.

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Section Six: Review Procedures: Ongoing Research
Date of Revision: 9/22/10

Introduction

HIRB oversight of research does not end upon approval of new research; instead, it continues for the duration of the study until the project is officially closed. Investigators are required to notify and secure approval of all amendments and changes to the approved research protocol and consent documents prior to implementing them, except in the event of an emergency in which participants' safety is in jeopardy. Investigators must also periodically submit progress reports to HIRB for continuing review so that HIRB can monitor the risks involved and require additional protections and changes as needed. HIRB determines the schedule for continuing review, which must be no less frequent than once per year.

Section Objective

This section contains policies and procedures regarding amendments and changes to previously approved research, continuing review of approved research protocols, and closure of studies.

Relevant Definitions

AUDIT Process by which HIRB examines a previously reviewed research protocol and research activities to date in order to ensure the continued protection of research participants and compliance with Federal, state, and local laws and regulations and HIRB policies and procedures.

BENEFIT Something that is useful to or improves the well-being of a participant or other individuals, such as treatment for a problem. Benefits can be direct or indirect. For instance, a direct benefit could improve participants' condition while an indirect benefit might improve scientific understanding of the condition but not directly alter it.

CONTINUING REVIEW The periodic oversight of human participant research projects by HIRB. At a minimum according to Federal regulations, HIRB must review every nonexempt study at least annually. HIRB reviews projects on at more frequent basis when necessary to ensure the protection of human participants [45 CFR 46.108(e)].

MINIMAL RISK When the probability and magnitude of anticipated physical or psychological harm or discomfort in the proposed research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests [45 CFR 46.102]. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of a routine physical examination.

MONITORING Process of collecting and analyzing information from ongoing research to ensure the protection of human research participants.

OHRP (OFFICE FOR HUMAN RESEARCH PROTECTIONS) An administrative office within the Department of Health and Human Services (DHHS). OHRP implements Federal regulations for the protection of human research participants [45 CFR 46] and provides guidance on ethical issues in biomedical and behavioral research.

PROTOCOL The formal design or plan of an experiment or research activity which is submitted to an IRB for review and often also used in applications to funding agencies. The protocol includes a description of the proposed research design and methodology, eligibility requirements for prospective participants, informed consent process, treatment regimen(s), and methods of analysis that will be performed on the data collected. The body of HIRB applications for new research consists of the research protocol.

RISK The possibility of physical, psychological, or social harm or injury resulting from participation in a research study. The likelihood and magnitude of possible harm varies from minimal to significant. Federal regulations define only one level of risk — minimal.

6.1 Amendments and Changes to Approved Studies

Federal regulations require that IRBs review and approve all proposed amendments and changes to previously approved research *before* the changes are initiated, except when necessary to eliminate apparent immediate hazards to participants. Investigators should use the Application for Amendments and Changes to request HIRB approval of proposed changes. (“Amendments” and “changes” are synonymous terms with respect to HIRB policies and procedures.) If a proposed change could affect participants’ willingness to continue involvement in the study, investigators may be required to re-consent all enrolled participants, using either an addendum to the original informed consent document or a revised consent document.

Initiating changes without prior HIRB review and approval is a violation of Federal regulations unless done to eliminate immediate hazards to participants. Investigators are reminded of this requirement in letters of HIRB approval, on the HIRB Web site, and in the Investigator’s Manual. If HIRB suspects that an investigator may have implemented changes without HIRB review and approval and cannot resolve the issue satisfactorily with the investigator, HIRB will conduct a for-cause audit (see Section 2.9). Suspicions may be based, for instance, on complaints from participants, indications of deviation in progress reports submitted for continuing review, and prior instances of noncompliance. The HIRB Chair may order the audit, or it may be passed as a motion by the full board. The audit may involve and is not limited to interviews with research team members and participants; observations of study procedures, including the informed consent process; and examination of study records.

Amendments and changes to approved studies MAY or MAY *not* alter the risk/benefit ratio for research participants, and these two conditions are subject to different review procedures as described below. The HIRB Director and/or Chair will review all proposed amendments and changes to determine whether they can be handled by expedited review or require evaluation by the full board.

Amendments and Changes that Do Not Alter the Risk/Benefit Ratio

Changes to approved studies that do not alter the study’s risk/benefit ratio are considered minimal risk changes. Such changes do not need to be evaluated at a convened full board meeting and may

be reviewed on an expedited basis by the IRB Director, one or more HIRB reviewers, or the HIRB Chair. Additionally, changes in research staff may be reviewed on an expedited basis by the IRB Administrator.

Examples of minimal risk changes:

- Changes in recruitment methods, such as revised advertisements.
- Study title changes.
- Changes in research investigators or research staff
- Minor changes in the Investigator's Brochure, for studies of investigational agents.
- Changes to improve the clarity of statements in consent documents.
- Minor changes in dosage or drug.
- Corrections to typographical errors in consent documents.

Amendments and Changes that May Alter the Risk/Benefit Ratio

Changes to previously approved studies that alter the risk/benefit ratio are considered greater than minimal risk changes and such changes must be reviewed at a convened meeting of the full board which meets once a month. Applications are placed on the board's agenda in the order in which they are received in the HIRB Office and sent to HIRB members at least one week prior to the full committee meeting.

Examples of changes that could alter the risk/benefit ratio and would qualify as greater than minimal risk changes if they did so:

- Changes in study design.
- Adding/requesting a Certificate of Confidentiality.
- Changes in sample size.
- The addition of an arm or population to the study.
- Changes in study eligibility criteria.
- Changes in research participants' status (e.g., some participants become incarcerated).
- Changes in the amount or type of specimens collected (e.g., blood).
- New information regarding the safety of a study drug or device.
- Major changes in dosage or drug.
- Major changes in the Investigator's Brochure, for studies of investigational agents.
- Adding audio-taping or video-taping of participants.

Guidance on Submission of Proposed Amendments and Changes

Investigators should adhere to the following when applying for approval of proposed amendments and changes:

1. The proposed amendment(s), the reasons for the amendment(s), and assessment of any risks or benefits to the participant and changes in the risk/benefit ratio that are associated with the change(s) should be clearly described in the Application for Amendments and Changes.
 - To speed review and provide clear records, two complete copies of the study protocol and/or other documents (e.g., consent forms, recruitment materials, and questionnaires) including all proposed additions, deletions, and other revisions, should be submitted. One copy should consist of the originally submitted version in which all proposed changes are highlighted or otherwise marked so they can be readily identified. (One option for accomplishing this is to use MS Word's "Track Changes" feature.) If the changes are *not* clearly indicated, the documents will be returned to the PI. The second copy should be an unmarked revision in which all changes have been made. (Selecting "Accept Changes" in MS Word can accomplish this.) If the revisions are approved, the clean copy will become the official copy on file in the HIRB Office.
 - The HIRB study number, revision date, and version number should be included on each page in the header or footer of all revised documents.
 - When submitting an amendment request to proceed with the next phase of a multi-phase study, the results to-date should be summarized, including the number of participants enrolled in the previous phase(s), knowledge gained from the previous phase(s), any unanticipated problems encountered and how they were resolved, and all safety monitoring reports (e.g., DSM, DSMB, and SMC reports).

HIRB Review of Requests for Amendments and Changes

The HIRB Chair and/or Director determines whether an Application for Amendments and Changes involves minimal risk or greater than minimal risk changes. Minimal risk changes are evaluated at the expedited review level, while greater than minimal risk changes require full board review.

HIRB determinations and motions for Applications for Amendments and Changes are the same as those for review of new studies; changes can be approved, approved pending minor revisions, deferred, or disapproved. Investigators are notified of these determinations and motions through letters from the HIRB Office.

6.2 Continuing Review

Federal regulations require periodic reevaluation of all approved research at intervals corresponding to the study's degree of risk but no less frequently than once per year for federally funded research. Research that does not involve federal funding may be reviewed less frequently per the HIRB's Flexibility Policy. HIRB satisfies this stipulation by requiring investigators to submit, on a set schedule, an Application for Continuing Review containing a progress report, which HIRB then reviews. Progress reports are required for all HIRB-approved active research projects (i.e., projects that have not been officially closed or terminated) even if all data analysis has been completed. If HIRB does not grant approval of the Application for Continuing Review by the continuing review deadline, HIRB approval of the project expires. A new Application for Expedited/Full Board Review is then required to continue the study.

The eHIRB system automatically sends continuing review reminders to PIs approximately 120 days prior to the deadline for continuing review, then weekly up to the expiration date. Investigators should submit an Application for Continuing Review at least 30 days prior to the deadline in order to allow sufficient time for processing the application prior to the expiration of HIRB approval. Continuing review applications submitted less than 30 days in advance may not meet the deadline for reapproval.

If the continuing review is not completed before the deadline, HIRB approval of the project expires, and the project is effectively terminated. No new participants may be enrolled, all ongoing research activities must stop, and participants currently participating must be notified that approval for the study has expired. Should investigators disregard this policy and continue research activities after expiration of HIRB approval, termination notices for noncompliance with HIRB policies will be sent to the PI, his or her department chair, the Institutional Official, Research Projects Administration Office and the Office of Human Research Protections (OHRP), if federally funded.

Deadline for Continuing Review

When HIRB first approves a research protocol, it sets the first deadline for continuing review. At the time of continuing review, HIRB sets the deadline for the next review.

The HIRB chair or member(s) who conduct expedited reviews may establish an annual deadline for continuing review for these studies. When the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may retain the anniversary date as the date by which the continuing review must occur.

Studies that are greater than minimal risk may be evaluated more often than annually. HIRB members establish the deadline for these studies on a case-by-case basis, taking into consideration the degree of risk and several other risk-related factors. Additional factors that are likely to cause HIRB to schedule continuing review more often than annually are:

- Inclusion of vulnerable populations.
- An investigator who has been found to be noncompliant on another study.
- Reports of unanticipated problems.
- Reports of noncompliance.
- Complaints about the study.

Specific Guidelines Based on Project Status

If enrollment is complete and contact with participants is ongoing or identifiable private data is in the process of being analyzed, the PI should do the following when submitting the Continuing Review Application:

- If a local or collaborating IRB in addition to HIRB is overseeing the research, include the latest statement of approval from the local or collaborating IRB. If the local or collaborating IRB does not review annually, indicate this in a separate memo.

If enrollment is complete and only unidentified data is being analyzed, the PI should submit only the Continuing Review Application.

HIRB Review of Applications for Continuing Review

In order for HIRB to approve an Application for Continuing Review, the research protocol and supporting documents must continue to meet the criteria set forth for approval of new studies, as required by Federal regulations [45 CFR 46.111].

Applications for Continuing Review are reviewed at the same level as the initial application for the study with several Federally-allowed exceptions. Research approved by the full board can undergo continuing review at the expedited review level in *any* of the following situations:

- The research is permanently closed to the enrollment of new participants, all participants have completed all research-related interventions, and the research remains active only for long-term follow-up of participants.
- No participants have been enrolled, and no additional risks have been identified.
- The remaining research activities are limited to data analysis.
- The research is not conducted under an IND application or IDE, and 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.

For expedited review, the application is forwarded to one or more designated HIRB members or the Chair for continuing review after HIRB Office staff members have confirmed the application's completeness. For full board review, complete applications are placed on the board's agenda in the order in which they are received in the HIRB Office. Application materials are sent to HIRB members at least one week prior to the full committee meeting. Those attending the meeting receive the application, which contains a progress report, consent documents if still in use, and recruitment materials if still in use. The primary reviewer receives all of the aforementioned materials and the up-to-date protocol, grant application, sponsor's protocol, questionnaires, and the Investigator's Brochure if an investigational device is being studied. (Expedited reviewers are considered primary reviewers and receive all of the materials listed for primary reviewers.) Upon request, the HIRB file and HIRB minutes for a specific study are provided to HIRB members.

HIRB determinations and motions for Applications for Continuing Review are the same as those for applications for new research. A continuing review application can be approved, approved pending minor revisions, deferred, or disapproved. Investigators are notified of these determinations and motions through letters signed by the HIRB Chair. When HIRB requests revisions, investigators should follow the procedures for submitting revisions listed in Section 5.11. Approval letters specify the expiration date for HIRB approval, a recommendation that Applications for Continuing Review should be submitted six weeks prior to the approval expiration date, a statement that changes cannot be implemented without HIRB approval, and a reminder that investigators must report unanticipated problems to HIRB. Copies of these letters are filed in the HIRB Office. When the research is funded, copies are sent to the Assistant Provost in the JHU Research Projects Administration Office.

At HIRB board meetings, studies that have been reapproved through expedited review since the previous meeting are reported to the board and entered into the meeting minutes. The Institutional Official is apprised of continuing review determinations and motions through distribution of the HIRB meeting minutes, as well as in regular meetings with the HIRB Director.

6.3 Closing Studies

Investigators are required to file a Study Closure with HIRB to formally inactivate their research protocol, eliminate the need for continuing review, and terminate HIRB approval. Final closure reports must be filed within 30 days of the completion of every IRB approved study (exempt research is not applicable). Investigators who fail to file final reports may be subject to sanctions including, but not limited to, required additional education and training or suspension of investigator privileges. It is the ultimate responsibility of the investigator to ensure that the final closure report is accurate and submitted in a timely fashion.

Circumstances warranting study closure include the following:

- The study has not been initiated and will not be undertaken.
- The study was stopped before completion to protect research participants. A copy of the DSMB or other safety monitoring reports, notification from the sponsor, or other documents that support the study's closure should be submitted with the Study Closure form.
- The study was stopped before completion because the investigators determined that the goals of the research could not be met. Investigators should explain this determination in their submission.
- The PI is terminating employment or association with the JHU Homewood Schools. The PI should specify whether she or he is transferring the research to a new institution. (Alternatively, the PI can transfer the study to another JHU Homewood Schools faculty or senior staff member through submission of an amendment application. Consent forms and other relevant documents with the new PI listed should be included for approval.)

Note: Transfer of a Federally-funded research project to a new PI usually requires the prior approval of the funding agency.

- Personnel from the Homewood Schools will no longer be engaged in a study headed by an outside PI.
- The study no longer requires HIRB approval because all recruitment and enrollment of participants, data collection, and analysis of identifiable private data is complete. To meet this requirement, there must be no more contact with participants and no access to or use of identifiable private data. Continued analysis of anonymized data (e.g., data stripped of identifiers, including codes) is permitted.

Retaining Records After Closure

Investigators are responsible for ensuring that all research records and correspondence are maintained appropriately and are available upon request to authorized Federal officials and JHU auditors throughout the course of the study and following the study's closure for at least three years. Records for studies involving individuals under 18 years of age must be retained until all participating individuals are at least 18, or for three years after the study closure, whichever is longer.

Investigators must maintain copies of all research proposals reviewed, scientific evaluations, approved sample consent documents, progress reports for continuing review, reports of unanticipated problems (which include injuries to participants), data safety and monitoring reports, and correspondence between investigators and HIRB. They must also maintain all signed consent documents in the manner approved by HIRB. All documents must be stored on campus in an office or in a document storage facility and should not be stored in private residences of investigators.

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Section Seven: Requirements for Specific Research Activities
Date of Revision: 12/17/14

Introduction

Some research activities warrant additional requirements and considerations in order to ensure the rights and safety of human research participants, including the confidentiality of their data. For instance, when JHU students are involved as investigators in research with human participants, the PI must be a faculty member. Other specific research activities that call for additional requirements and considerations include research at international sites, research in educational settings, research via the Internet, research with human biological materials, program evaluation, oral history studies, self-experimentation, research supported by grants and contracts, pilot activities, multi-site studies, studies transferred to JHU, and research without a definite plan to involve human participants.

Section Objective

In this section, additional requirements and considerations for specific research activities are presented. These requirements and considerations are designed to augment protection of the rights and welfare of human research participants.

Relevant Definitions

CLASS PROTOCOL Description of research to be undertaken by students in a class or classes to learn more about the process of research and to satisfy course objectives. An instructor must serve as the PI.

CONFIDENTIALITY Refers to the privacy of human research participants and efforts to control access to information related to their participation in order to protect their privacy.

COORDINATING CENTER An entity that organizes multi-site studies. Coordinating centers that receive or possess individually identifiable (either directly or through coding systems) private information for research purposes are considered to be engaged in research.

FEDERALWIDE ASSURANCE (FWA) A written, binding commitment submitted to OHRP by an institution engaged in human participant research in which the institution promises to comply with applicable Federal regulations governing such research and specifies the procedures it will follow to ensure compliance [45 CFR 46.103]. The Johns Hopkins University Homewood Schools' Federalwide Assurance is No. 00005834.

FERPA (FAMILY EDUCATIONAL RIGHTS AND PRIVACY ACT) A Federal law protecting the privacy of students' school records [34 CFR Part 99]. [<http://www.ed.gov/policy/gen/guid/fpco/ferpa/index.html>]

INDIVIDUAL STUDENT RESEARCH A study undertaken by an individual student, such as a thesis or dissertation, in collaboration with a faculty member. The faculty member must serve as the PI.

OHRP (OFFICE FOR HUMAN RESEARCH PROTECTIONS) An administrative office within the Department of Health and Human Services (DHHS). OHRP implements Federal regulations for the protection of human research participants [45 CFR 46] and provides guidance on ethical issues in biomedical and behavioral research.

PILOT ACTIVITIES Small-scale studies to refine a research design, determine the feasibility of a larger study, or test a research instrument. (Also referred to as **PILOT STUDIES** and **PILOT RESEARCH**.)

PPRA (PROTECTION OF PUPIL RIGHTS AMENDMENT) The Protection of Pupil Rights Amendment (PPRA) (20 USC § 1232h; 34 CFR Part 98) applies to programs and schools that receive funding from the U.S. Department of Education (ED). It requires that schools and contractors obtain written parental consent before minor students are required to participate in any ED-funded survey, analysis, or evaluation that involves protected information [<http://www.ed.gov/policy/gen/guid/fpco/ppra/index.html>].

REPOSITORY A storage site and/or mechanism for collecting, storing, and distributing human biological materials for research purposes.

STATISTICAL CENTER An organization that processes data. Statistical centers that receive or possess individually identifiable (either directly or through coding systems) private information for research purposes are engaged in human participant research.

7.1 Class Projects

Classes in the Homewood Schools may give enrolled students the opportunity to work on research projects involving human participants. Although these class projects may not meet standard definitions of research (e.g., results that will contribute to generalizable knowledge), the potential for risk to human participants requires that HIRB review all such projects. The review process also helps familiarize students with the ethical framework for human participant research and sound research practice.

Instructors may be able to obtain HIRB approval of multiple class research projects through submission of a single application. Instructors must serve as the PIs. Instructors should describe the multiple class research projects within the standard application. Instructors are encouraged to contact the HIRB before submitting a class research project to discuss how to submit.

Note: Individual student research projects, such as honors theses and doctoral research, do not qualify for use of the class protocol. Individual student research projects involving human research participants that are conducted through independent study or as part of graduate work require the preparation of an application in collaboration with a faculty member..

Policies and Procedures

When instructors propose to include human research participants in class activities, they may submit a request for the approval of a class protocol if **all** of the following apply:

- The objective is for students to learn how research projects are designed and conducted.
- Data analysis will occur only for class purposes.
- The proposed student projects are very similar to each other in both content and design.

Projects eligible for the Class Protocol Application must adhere to the following guidelines:

- The instructor assumes primary responsibility for ensuring that the rights and welfare of human research participants are protected and high standards of research ethics are maintained. All instructors must complete the required human participant research training module before their classes undertake human participant research. (See Education Requirements below.)
- Projects are substantially similar to each other, with only minor variations in content and design. For example, students may conduct survey research by selecting questions from a single large survey instrument. In most cases, projects will fall into only one of the categories for either exempt research or expedited review.
- Students may only draw research participants from a population of individuals 18 years of age and older and may not include vulnerable populations.
- Projects may not include any personal, sensitive, or incriminating topics or questions that could place participants at risk.
- Projects may not include manipulation of participants' behavior beyond the range of normal classroom activities or daily life.
- Projects may not involve physically or psychologically invasive contact with participants.

HIRB may require revisions in participant population, topic areas, and procedures to ensure the protection of study volunteers. Projects that do not follow the above guidelines, including those that involve sensitive topics or vulnerable populations, are not eligible for a class protocol.. Projects addressing more sensitive topics or involving vulnerable populations must be submitted as individual student research projects, with a faculty member supervising the research and serving as the PI.

Note: Instructors planning to submit a Class Protocol Application are strongly encouraged to contact HIRB as soon as possible for additional guidance on choosing class research projects that satisfy the criteria for a class protocol.

Education Requirements

All instructors and students who will be involved in human participant research must complete the Johns Hopkins University [Collaborative Institutional Training Initiative \(www.citiprogram.org\)](http://www.citiprogram.org) computer-based human participant research training program. This requirement applies regardless of whether the research is funded or not and irrespective of the funding source or where the research is performed.

Upon successful completion of the required modules, instructors and students should print a copy of the available certificate as evidence of their successful completion of training in human participant research. Instructors must complete the training prior to submitting an application to HIRB. Students must complete the required training prior to their involvement in the research. (For more details on HIRB education requirements, see Section 4.)

7.2 Individual Student Research Projects

Students in the JHU Homewood Schools have the opportunity to engage in a variety of research activities, including individual student research projects such as honors theses, independent study

projects, graduate theses, and dissertation research. Individual student research projects may include human participants. Although in some cases these research projects may not meet standard definitions of research (e.g., results that will contribute to generalizable knowledge), the potential for risk to research participants requires that HIRB reviews them.

The review process helps familiarize students with the ethical framework for human participant research and sound research practice. However, students (undergraduate and graduate) may not serve as PIs. All student applications must have a faculty member who will serve as PI and assume responsibility for overseeing the research.

Note: Student research projects involving human participants that are conducted as a class activity may be eligible for approval as a class protocol.

Education Requirements

Students who plan to conduct an individual research project with human participants must complete the Johns Hopkins University [Collaborative Institutional Training Initiative \(www.citiprogram.org\)](http://www.citiprogram.org) computer-based human participant research training program. This requirement applies regardless of whether the research is funded or not and irrespective of the funding source or where the research is performed. The faculty PI also must complete the training program before submission of the application to HIRB.

Applying for HIRB Review

Students planning to conduct human participant research are urged to begin the application process with their faculty PI as early as possible to allow ample time for preparation and review of their HIRB application. This is especially true of international research. HIRB recommends submitting a complete application at least three months in advance of when international research is scheduled to begin. (See Section 7.3 for more details on international research.)

As outlined below, faculty supervisors are responsible for assisting their students with the HIRB review process and for checking all HIRB application materials for accuracy and completeness. Incomplete or inaccurate applications will be returned to the faculty supervisor without review.

Faculty Supervisor Responsibilities

Faculty members who serve as a PI for an individual student's research project are expected to work closely with the student in preparing the application for HIRB review, overseeing the conduct of the research, and ensuring that the study is appropriately closed upon completion. More specifically, faculty supervisor responsibilities include, but are not limited to, the following:

- Thoroughly reviewing materials to ensure that a complete and accurate application is submitted to HIRB.
- Ensuring that the student completes the required training in human participant research and has the appropriate knowledge and skills to carry out the research in a manner that protects all participants.
- Monitoring the conduct of the research project to ensure that the student fulfills the following responsibilities:

- a. Obtaining and documenting the informed consent of each participant or each participant's legally authorized representative (LAR), unless HIRB has waived these requirements. This includes ensuring that each potential participant understands the nature of the research and, unless HIRB specifically waives this requirement, each participant or the participant's LAR receives a copy of the HIRB-approved informed consent document at the time of consent.
 - b. Retaining all signed consent documents for at least three years after the completion of the study according to institutional policy.
 - c. Promptly reporting proposed changes to the research protocol or consent documents to HIRB. The proposed changes may not be initiated without HIRB review and approval, except where necessary to eliminate apparent immediate hazards to participants.
 - d. Promptly reporting to HIRB any unanticipated problems involving risks to participants or others.
 - e. Promptly reporting to HIRB any serious or continuing noncompliance with Federal regulations or HIRB policies and procedures.
 - f. Informing HIRB of any new personnel to be added to the research team.
 - g. Ensuring that all members of the research team have completed the required training in the protection and ethical treatment of human research participants and have been appropriately trained for their role in the study.
 - h. Ensuring that all members of the research team report any potential conflicts of interest regarding the research.
 - i. Reporting on the progress of approved research to HIRB as often as and in the manner prescribed by HIRB. This includes complying with all requirements for continuing review.
- Ensuring that HIRB is notified when the individual student's research project is complete so that the study may be appropriately closed.

7.3 Research at International Sites

HIRB recognizes the value and complexity of international research projects. Investigators should be aware of the special review requirements for international human participant research and should submit their applications to HIRB at least three months prior to when they plan to begin data collection in a foreign country.

Investigators working in foreign countries should take the local norms and culture into consideration when developing their protocol for human participant research. Without this knowledge, researchers may inadvertently put their participants at risk. For instance, in some countries people are not allowed to talk about their government, either positively or negatively. Asking government-related questions could put such participants at risk. A critical responsibility of the researcher is to know the population under study and to ensure that HIRB is provided with information about the local context from an authority who is not affiliated with the researcher's project. This information should include assessment of whether the research topic is of a sensitive

nature, what local laws must be followed, potential risks to participants, and what methods for collecting data and ensuring confidentiality are appropriate for the region. Alternatively, approval by a local IRB, Ethics Committee (EC), or government authority can be substituted for the provision by an independent expert of the information specified above.

Federal Regulations

Federal regulations in the U.S. recognize that research protections in foreign countries may differ from those in the U.S. The foreign country's procedures may be substituted for the procedures required in the U.S. if the foreign country's procedures afford protections that are at least equivalent to those in the U.S. and HIRB approves the substitution following review of the foreign procedures.

It is sometimes difficult to determine what constitutes "protections that are at least equivalent" to the Federal regulations. This determination may need to be made by the Office for Human Research Protections (OHRP). The broad policy outlines of international standards, such as the *Declaration of Helsinki* and *The Nuremberg Code*, are a starting place but are insufficient. Written descriptions of the procedures developed from such policies and adopted by the foreign country are required.

Recognizing the continuing growth of international research, OHRP has developed an International Compilation of Human Subject Research Protections. The compilation lists the laws, regulations, and guidelines of over 50 countries where research that is funded or supported by DHHS is conducted. The compilation provides direct web links to each country's key organizations and laws, when available. OHRP believes this compilation will assist IRBs, researchers, and others to ensure that international studies comply with applicable foreign laws. The compilation can be accessed on the OHRP Web site [<http://www.hhs.gov/ohrp/international/HSPCompilation.pdf>].

Local Approval

Applications for HIRB approval of international research should identify whether there is a local IRB, Ethics Committee (EC), or government entity that will review the study in the host country. If local review has been conducted, a copy of the approval letter or notice should be included with the HIRB application. If local review has not yet been initiated or is in process, this should be made clear in the application.

There are countries in which a local review board or government review entity is not available. In such cases, HIRB must obtain a consultation from an individual who is familiar with the cultural background, local context, and community attitudes of the country in which the research will be conducted in order to ascertain whether the research is appropriate. The PI needs to identify the local expert and provide contact information to the HIRB Office. This individual may not be associated with the conduct of the proposed research. HIRB Office staff will then contact the identified individual and obtain information about the local context. Specifically, HIRB staff will ask the local expert what local laws must be followed, whether the proposed recruiting and consent procedures are appropriate for the local population, whether study procedures could jeopardize participants' safety, and if the expert has any other concerns about the research.

Note: HIRB will not approve an international study unless it has (1) received documentation that local review and approval has been granted in the host country or (2) consulted directly with a local expert.

Informed Consent

While U.S. standards for documentation of informed consent should not be forced upon other cultures, HIRB standards for the ethical conduct of research and a meaningful consent process should not be relaxed. Special attention should be given to local customs and cultural and religious norms in drafting consent documents or proposing alternative consent formats. In some instances, it may be appropriate for HIRB to waive some or all requirements for written consent. Research proposals for which this may be reasonable should include explanations of cultural norms or conditions requiring such a waiver (e.g., societies where no written language is used, societies where signatures represent the surrender of spirit or soul to the researcher).

Requests for waiver or alteration of informed consent will be considered if the protocol including the consent process that requires waiver or alteration has received local approval. If a local expert is required, the expert will be asked to comment on the proposed consent process. HIRB reserves the right to make the final decision whether to waive or alter informed consent requirements, including documentation of informed consent. HIRB requires consent forms (and oral consent scripts if applicable) to be written at a level and in a language that will be understandable to the participant population. (See Section 8.9 regarding the informed consent of non-English speaking participants.)

Additional Considerations

Investigators should consider the following when preparing their applications for HIRB approval of international research:

- PIs are responsible for the appropriate education and conduct of those conducting the research, both paid personnel and volunteers in the U.S. and the foreign country. Educational requirements for research team members in international studies are the same as in U.S. studies. Training programs and certificates of education may require translation.
- Recruitment materials in both the language of the host country, when not English, and in English should be included in the HIRB application.
- Participants should be informed if they will have access to a treatment locally following study completion.
- In the U.S., acceptable standards of data safety include password protection, locked file cabinets, and removal of identifying information. In a foreign country, investigators should consider the available facilities and technologies for the security of the data while they are in that country and whether the data could put participants at risk if confidentiality is breached. Investigators should also consider the best mode for transporting data back to the U.S. Locked containers are no longer allowed on airlines. It may be safer to send the data by mail or in the possession of a research team member.
- Proposed payments to participants should be described in terms of both U.S. and local currency. A description of payment in relative terms (i.e., payment equals a day's work, hourly salary, or another local reference) is recommended.

- Participants must be provided with the phone number of a local investigator or a local IRB/EC representative who can answer research-related questions. If the project is a clinical trial, local emergency contact phone numbers must be included.

7.4 Research in Educational Settings

Research in public and private schools requires review and approval not only by HIRB but also by the school or school system. Investigators must provide HIRB with a letter of cooperation from an appropriate school or school system official. Many school systems have a research division, office, or committee that reviews outside research proposals and provides a letter of cooperation upon approval. If the school or school system does not have an established review system, investigators should request approval from appropriate individuals such as school principals.

In addition, investigators collecting data in public schools, or private schools that receive Federal money, must take into account the Family Educational Rights and Privacy Act (FERPA) regulations when seeking private identifiable school records. FERPA controls access to and disclosure of personally identifiable student information and records. The Protection of Pupil Rights Amendment (PPRA) controls the development and administration of surveys that involve protected information in local educational agencies (i.e., school systems) and schools. Investigators are responsible for ensuring that the school or school system is in compliance with FERPA and PPRA. The letter of cooperation from the public school or school system official should include a statement that the school complies with FERPA and PPRA, in addition to a statement that the school or school system supports the research.

Under FERPA, with certain exceptions, the permission of parents or guardians must be obtained before students' records or personally identifiable information is disclosed. Under PPRA, the permission of parents or guardians must be obtained, or in some cases the parents or guardians must be allowed to exclude their children, if an investigator develops or administers a survey for students that covers one of the following areas of protected information:

1. Political affiliations or beliefs of the students or students' parents.
 - Mental or psychological problems of the students or students' family.
 - Sexual behavior or attitudes.
 - Illegal, anti-social, self-incriminating, or demeaning behavior.
 - Critical appraisals of individuals with whom the students have close family relationships.
 - Legally recognized privileged or analogous relationships, such as those with lawyers, physicians, or ministers.
 - Religious practices, affiliations, or beliefs of the students or students' parents.
 - Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such a program).

Obtaining informed consent may be especially difficult when recruiting students from schools. It is imperative that investigators obtain signed parental permission prior to obtaining assent from students. This may be accomplished by giving students letters containing permission forms to take home to their parents.

More information regarding FERPA can be found online [<http://www.ed.gov/policy/gen/guid/fpc/ferpa/index.html>]. More information on PPRA also can be found online [<http://www.ed.gov/policy/gen/guid/fpc/ppra/index.html>].

7.5 Research via the Internet

The Internet offers unique opportunities for researchers to study social and behavioral interactions in a virtual environment and presents new IRB-related challenges. Although Federal regulations do not address research on the Internet, investigators and HIRB should adhere to these basic review criteria when designing or evaluating this type of research:

- Risks are minimized and offset by anticipated benefits.
- Selection of participants is equitable.
- Informed consent will be obtained from all prospective participants and will be appropriately documented.
- Adequate provisions are made to protect the privacy of participants and maintain confidentiality of their data.
- There is a DSM, DSMB, or SMC, if appropriate.
- Additional safeguards are included to protect vulnerable populations.

Researchers should specifically address the preceding points when submitting a HIRB application for Internet research. The ethical principles of respect, beneficence, and justice apply to research conducted on the Internet just as they do to more traditional methods.

Recruitment Process

It is usually inappropriate to recruit participants directly from Internet discussion groups, chat rooms, etc., as this may constitute an invasion of privacy. Acceptable recruitment methods include posting notices on bulletin boards and asking Listserv Managers to distribute announcements to their members.

All research involving human participants should include a broad range of populations to ensure that all persons share in the benefits and bear the burdens of the research. Unless the research justifies a more restrictive sample, investigators should consider the recruitment methods necessary to attract participants who are diverse in terms of race/ethnicity, gender, and economic status in order to avoid the limitations of nonrepresentative sampling. Investigators should consider how recruitment via the Internet might skew their sample.

If the research will not involve children, researchers must develop a plan for screening out minors. Monitoring software and adult check systems, although not foolproof, can be used. If the research will involve children, investigators must incorporate the additional safeguards (e.g., child assent, parental permission, etc.) for children that are required by Federal regulations and HIRB policies and procedures. (See Section 11.1 for information about research involving children.)

In their HIRB applications, investigators should:

1. Describe the recruitment process.

- Will a mailing list be used to send an announcement to individuals' e-mail addresses? If yes, what is the source of the mailing list?
- Will a Webmaster or Listserv Manager post an announcement? If yes, provide evidence of approval from that person.
- Explain how potential participants will respond to the advertisement.
- Will potential participants respond via e-mail or post office mail or be directed to a Web site?

*Note: **all** advertisements, including Internet-based ads, must be reviewed and approved by HIRB prior to their use.*

Risks and Benefits

Two major sources of harm in conducting research on the Internet arise from the lack of direct contact with participants and the potential for breaches of confidentiality. Indirect contact with participants may not allow researchers the opportunity to deal with participants' reactions to certain situations, or, because of the fluid nature of virtual communities, to follow-up with participants. Participants' questions may go unanswered, and participants' negative psychological reactions to the research may be undetected and unaddressed.

Conducting research on the Internet is not likely to cause physical injury, but it may increase the risk that participants' identities will be exposed. The identity of participants and personal information about them may unknowingly be disclosed during data gathering, data processing, or data storage. Clearly defined technical information regarding confidentiality that is easily understood by a broad range of persons must be in place when interacting with participants. To the extent possible, protections should be developed to guard against inadvertent disclosure of identity.

Internet research also raises concerns that data collection problems may weaken the validity of the data collected. Problems created by pseudonyms, multiple submissions, and overt deception warrant special consideration.

In their HIRB applications, investigators should address the following questions:

1. How will responses from individuals not intended to be in the sample be screened out?
 - How will multiple submissions be detected and screened out?
 - How will accuracy of the data be ensured?

Informed Consent

Researchers must address how informed consent will be obtained and authenticated. The written consent of all participants or their legally authorized representative (LAR) must be obtained unless HIRB grants a waiver. Documentation of consent may include use of a procedure in which participants must click a consent page that includes all of the elements of informed consent before accessing the survey. Another option is for participants to print a consent documentation page that they sign and send by mail to the researcher. Then the researcher, upon receipt of the signed consent documents, gives participants access to the survey.

In their HIRB applications, investigators should address the following questions:

1. What is the process for obtaining consent?
 - Will a waiver or alteration of the informed consent requirements be requested from HIRB?
 - If children will be involved in the research, how will parental permission be obtained? HIRB grants a waiver for obtaining parental permission only in limited circumstances.
 - What is the process for ensuring participants' understanding of the research?
 - What is the process for answering any questions participants have about the research?
 - How will consent be documented?
 - Will a waiver of informed consent documentation be requested from HIRB?
 - How will informed consent be validated? In other words, how will the identity of participants be verified?

Confidentiality

Confidentiality of sensitive data may not be as easily protected in Internet research as in more traditional research. Researchers should provide HIRB with their plans for ensuring confidentiality of the data during each stage of research: gathering, processing, and storage. In addition, safeguards should be in place for protecting against inadvertent disclosure and deliberate attempts to gain access to the data.

Data transmitted via the Internet often is not anonymous. The sender's email address is contained in almost all email formats. Cookies, which are small files often left on a user's hard drive, are sent back to a web-site each time a page is requested from that site. Cookies record computer information, details of accessed links, and even email addresses. Participants may be unaware that online interactions may be stored in the cache memory or server's log files. Researchers may use a third party to strip email addresses and other identifying information, or they may develop screen warning messages, disclosing the limits of security.

In their HIRB applications, investigators should address the following questions:

1. Will the survey contain identifiers, or will it be anonymous? Will a third party strip identifiers (e.g., e-mail addresses)?
 - How will the data be transmitted to the server, and what measures will be taken to ensure data security during transmission?
 - How will data be stored and secured?
 - What technical information regarding confidentiality, if any, will be given to participants preceding online data collection?

Web Site Content

The content of the information contained on a website or distributed to potential participants must be reviewed and approved by HIRB. A hard copy of the information to be broadcasted must be submitted with the HIRB application, along with the website address.

7.6 Research with Human Biological Materials

HIRB oversees the collection, storage, and use of human biological materials when these activities qualify as human participant research. Examples of human biological materials are cells, organs, blood, urine, excreta, saliva, amniotic fluid, placenta tissue, hair, nail clippings, and teeth. Research activities include human participants when they involve (1) an intervention or interaction with a living individual that would not occur, or would occur in some other fashion, if not for the research OR (2) identifiable private data or information to be used in a form that could be associated with a living individual. For example, research that uses human cell lines where the donor(s) may be identified, including cells that retain links (such as codes) to identifying information, is generally considered human participant research and, thus, requires IRB review.

HIRB does not oversee the storage or management of human biological materials that are collected and stored solely as part of routine clinical care or hospital procedures. HIRB also does not oversee the use or management of specimens or data sent to Homewood personnel for specialized analysis as part of a contractual agreement, unless the Homewood personnel intend to use the specimens or data for research purposes. Activities do not include human research participants when biological materials are collected in their entirety for purposes other than research or submission to a repository (e.g., the material is collected solely for clinical purposes, with no “extra” material collected for research or submission to a repository) and the materials are without any identifiable private data or information (i.e., no codes or links of any sort are maintained that would permit access to identifiable private data or information about the living individual from whom the material was obtained). For example, in vitro research and research in animals using already derived and established human cell lines from which the identity of the donor(s) cannot readily be ascertained by investigators are not considered human participant research and do not require IRB review.

Investigators may be interested in contributing to, establishing, or extracting specimens or data from a repository for human biological materials. A repository is a storage site and/or mechanism for collecting, storing, and distributing human biological materials for research purposes. Repository activities have three components: (1) the collection of tissue samples, (2) the operation of the repository, and (3) the receipt of materials by investigators. Each component may be subject to IRB review. For instance, an IRB would need to review and approve a protocol specifying the conditions under which data and specimens may be accepted and shared, ensuring adequate provisions to protect the privacy of participants and maintain the confidentiality of data. A Certificate of Confidentiality might be needed to protect confidentiality of repository specimens and data. The IRB overseeing the repository also would need to review and approve a sample collection protocol and informed consent documents for those who collect human biological materials for the repository. The collectors’ local IRBs would then need to review and approve the collection protocol and consent documents.

Investigators interested in conducting research with human biological materials are encouraged to contact the HIRB Office to discuss their plans and learn more about Federal regulations governing this type of research.

7.7 Program Evaluation

Program evaluations, including quality improvement activities, require HIRB review when they involve human participants and meet the Federal definition research — in other words, when they

constitute a systematic investigation designed to develop or contribute to generalizable knowledge. If the results will be published in an academic journal, the study should likely undergo HIRB review. If the evaluation will inform the development or implementation of other external programs, it likely requires HIRB review. Also, if the evaluation will inform public policy or affect the replication of other programs, it likely needs HIRB review. The following are examples of program evaluations that require HIRB review:

- Head Start programs are evaluated to determine whether they improve children's academic achievement and deserve public funding.
- The components of a nationally disseminated pregnancy prevention program with proven effectiveness are studied to identify which are essential for program success.

When program evaluations do not meet the definition of human participant research, they do not require HIRB review. Therefore, when program evaluation data are collected for internal purposes, HIRB review generally is not needed. The following are examples of program evaluations that do *not* require HIRB review:

- A needs assessment is conducted to determine if a specific program is needed at a particular institution.
- An institution examines the demographic characteristics of individuals accessing certain services and individuals' satisfaction with those services.

7.8 Oral History Studies

Oral history studies require HIRB review when they involve human participants and meet the Federal definition of research — in other words, when they constitute a systematic investigation designed to develop or contribute to generalizable knowledge, including the creation of a collection for other researchers. The following are examples of oral history studies that require HIRB review:

- Open-ended interviews are conducted with veterans of the Gulf War to document their experiences, draw conclusions about their experiences, and inform policy.
- Structured interviews with female politicians are videotaped in order to create an archive for future research.

However, often oral history interviews are collected from individuals selected because of their unique relationship to a topic in order to gather particular perspectives on the topic that are not necessarily generalizable or to document a specific historical event without drawing conclusions, generalizing findings, or informing policy. Oral history research which seeks to record and archive historical experiences and to explore memory and meaning in narratives rather than to systematize interview data into general sociological or scientific knowledge likely do not meet the definition of human participant research and therefore are not subject to Federal requirements governing human participant research and do not require review by HIRB.

The following are examples of oral history studies that do *not* require HIRB review:

- Videotaped interviews are conducted with Holocaust survivors to create an historical record of specific personal events and experiences.

- Videotaped interviews with World Trade Center survivors are created for viewing in a museum in order to provide a historical record of specific personal events and experiences related to the attack and provide a venue for survivors to tell their stories.

7.9 Expert Opinions

Researchers sometimes solicit the opinions of experts through phone or face-to-face interviews, surveys, and panel discussions. Experts are persons who, by virtue of their training or expertise, have information and knowledge in a substantive area beyond that of the average person and who regularly share this information and knowledge through consultation, teaching or public speaking, or publications and written reports. For HIRB purposes, experts are not human subjects when asked to provide information and opinions within their areas of expertise. Communications with experts on non-private information do not require HIRB approval.

7.10 Autobiography or "Auto-ethnography"

In sociology, anthropology and related disciplines, postmodern ethnography, autobiography, or auto-ethnography is a narrative method in which the investigator and "subject" are one and the same. That is, the investigator reports on his or her personal experiences and perspectives. In this form of narrative reporting, the investigator is not considered a research subject, and HIRB approval is not required.

7.11 Self-Experimentation

Federal regulations do not distinguish between self-experimentation and research on participants who are recruited for a specific project. Faculty or students who participate in self-experimentation should consider themselves human participants involved in research that requires HIRB approval when the experimentation meets the Federal definition research — in other words, when it constitutes a systematic investigation designed to develop or contribute to generalizable knowledge. Reflective methods, such as journaling, to improve teaching or other aspects of one's job performance do not require HIRB approval.

7.12 Pilot Activities

Pilot activities include small-scale studies to refine a research design, determine the feasibility of a larger study, or pilot test a research instrument. Pilot activities that must be reviewed by HIRB are those in which an investigator (1) systematically collects data through intervention or interaction with one or more living individuals or (2) obtains identifiable private information about one or more living individuals that is intended to develop or contribute to research.

Refining a questionnaire through feedback obtained from a small group of individuals in preparation for a larger study is an example of a pilot activity that requires HIRB review. On the other hand, casually asking a colleague to check a research instrument for understanding is not human participant research and does not need HIRB review. Investigators who are uncertain as to whether a planned activity requires HIRB review are encouraged to consult the HIRB Office.

7.13 Multi-Site Studies

In many studies, data is collected outside the Homewood Schools, which qualifies the research project as a multi-site study. Specific requirements apply to Non-JHU sites, as explained below. Some multi-site research projects rely on a statistical or coordinating center. When a statistical or coordinating center is located in the Homewood Schools, specific requirements apply.

Non-JHU Sites

When a Homewood investigator plans to conduct research at any site not under the control of JHU (e.g., an elementary school, homeless shelter, nursing home, other universities, etc.), the following information must be provided to HIRB: name of the site, address of the site, name of a contact at the site, and contact information (e.g., phone number and e-mail).

In the HIRB application, investigators should also address the following questions:

- Has the site provided permission to conduct the research at that site?
- Is the site engaged in the research?
- If engaged in the research, does the site have an IRB?
 - a. If the site has an IRB, has the site's IRB approved the research?
 - b. If the site has an IRB, does the site want to depend on HIRB for IRB approval?
 - c. If the site does not have an IRB, is an Individual Investigator's Agreement needed?

Before HIRB grants final approval of the research protocol, HIRB Office staff will ensure that all non-JHU sites have provided permission to conduct the research at those sites. If the site has an IRB, the IRB must either approve the research or defer approval to HIRB. If the participating site is actively involved in the conduct of research and would like to defer approval to HIRB, HIRB must formally become the IRB of Record. If the participating site is actively involved in the conduct of the research and does not have its own IRB, an Individual Investigator's Agreement may be needed.

HIRB final approval will be withheld until HIRB has all necessary approvals, agreements, and other documentation on file. If any problems arise with external sites, HIRB Office staff will communicate with the contact person named in the application.

Statistical and Coordinating Centers

Statistical and coordinating centers typically are responsible for general oversight of the conduct of a research project, data management, and communication among the multiple sites participating in the research. Statistical and coordinating centers may be designated by a sponsor or by mutual agreement of participating sites.

There are two possible ways to address statistical and coordinating centers located in the Homewood Schools.

1. The statistical or coordinating center PI will submit a specific protocol to HIRB for the center that outlines the responsibilities of the center. It will not include local site protocol information, even if data are going to be collected by the same PI and/or other Homewood investigators, in which case a separate application will be submitted. The statistical or

coordinating center protocol must be submitted to HIRB for review and approval prior to the initiation of center activities.

- A Homewood PI will serve as the statistical or coordinating center PI and as the local PI for the multi-center study. There will be a local site protocol that describes the study into which participants will be enrolled, and a specific statistical or coordinating center protocol will not be submitted. Instead, the statistical or coordinating center functions will be described in the local site protocol and consent documents. HIRB will review these documents to determine if the center functions are adequately described.

In either case, investigators must provide HIRB with a description or evidence of the following:

- Each participating site's local IRB approval and consent forms,
- Confirmation that each site has an FWA on file with OHRP.
- A method for assuring that all sites have the most current version of the research protocol.
- A plan for the collection and management of data from all sites.
- A system to confirm that amendments to the protocol will be communicated to all sites, and the process for reporting and evaluating unanticipated problems and protocol deviations at all sites.

7.14 Studies Transferred to JHU

Newly appointed investigators in the Homewood Schools who wish to transfer a research project from their former institution to JHU should submit the following to the HIRB Office: a copy of the entire grant or contract (if applicable), the IRB-approved research protocol, a current statement of approval from their former IRB, consent documents, and all research instruments, as well as a cover letter that includes the investigator's telephone number and e-mail address. HIRB will review this information and determine if a new HIRB application must be submitted or the approval of the investigator's previous IRB can be substituted for HIRB approval.

If HIRB determines that the study can be transferred in its existing state with the previous IRB approval in effect, the investigator must complete the required human participant research training program (see Section 4) and submit a HIRB application for new research prior to expiration of the current approval period set by the previous IRB.

All newly appointed faculty who plan to conduct human participant research are encouraged to contact the HIRB Office to review HIRB policies and procedures.

7.15 Research not requiring HIRB review

In some cases researchers may be involved in inquiries that, while involving the participation of other individuals, do not constitute research that requires review by the HIRB. Where the participation of these individuals does not pose any risk of civil or criminal liability or the potential to damage the participants' financial standing, employability or reputation and the individual is not the subject of the research the project may not require HIRB review. These types of research typically include areas of inquiry where the information provided by the participants is not about himself or herself but rather about a process, policy, or other topic that is the subject of the research. For example, in poli-

cy evaluations a researcher may conduct a survey or focus group on the success or failure of public policy that has been enacted with the goal of recommending changes to the policy. Another example would be a researcher investigating ways to improve marketing strategies for an organization. In both of these cases the input solicited about the process is not private information and the subject of the research is not the individual.

7.16 Research Supported by Grants or Contracts

HIRB is required to review and approve all new grants and contracts for research that involve human participants, in addition to reviewing and approving the respective application for exemption or expedited or full board review. Investigators who have applied for a grant or contract can submit an application for new research, in which they note the grant or contract application. However, HIRB will not review grant or contract proposals unless they have received a high priority score or been awarded funding.

For grant and contract proposals that have received a high priority score or been awarded funding, investigators must submit the entire grant or contract, with individual salaries blocked out, even if the research qualifies as exempt. HIRB will review the grant or contract and complete a Grant/Contract Review Checklist. Once approved, the HIRB Office will forward copies of the first five pages of the proposal, the statement of approval, and the Grant/Contract Review Checklist to the Research Projects Administration Office. The Research Projects Administration Office will not issue a budget number or release funds until it has verified that HIRB has approved both the application approval of new research and the grant or contract proposal.

7.17 Research Without a Definite Plan to Involve Human Participants

Certain types of applications for grants or contracts are submitted to departments or funding agencies with the knowledge that human research participants may be involved within the period of support but without a definite plan for their involvement set forth in the application. These applications include institutional grants in which selection of specific projects is the institution's responsibility; research training grants in which the activities involving participants are to be selected later; and projects in which human research participants' involvement will depend upon the completion of instruments, prior animal studies, or purification of compounds. HIRB does not need to review these applications before an award is made. However, no human participants may be involved in any project supported by these awards until the project has been reviewed and either exempted or approved by HIRB and certification submitted by JHU to the supporting department or funding agency.

In the event that research is undertaken without the intention of involving human participants, but the investigators later decide to include them, HIRB must review and either exempt or approve the research *before* contact with potential participants is initiated.

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Section Eight: Informed Consent Process
Date of Revision: 11/16/14

Introduction

Informed consent is a process rather than a document signed at a discrete moment in time. The informed consent process is essential for the ethical treatment of research participants. It protects and demonstrates respect for potential participants. Sufficient information is provided to enable autonomous individuals to understand their rights with respect to the study and the research procedures, risks, and benefits so that they can make an informed decision about whether to enroll. The informed consent process also protects potential participants who lack the capacity to provide informed consent on their own.

Section Objective

The objective of this section is to describe the informed consent process, including the elements of informed consent that Federal regulations require, waivers of informed consent, and tests of understanding. In addition, the informed consent process for the following populations is detailed: children, decisionally-impaired adults, non-English speakers, participants contacted via phone, and secondary participants.

Relevant Definitions

ASSENT Affirmative agreement by an individual who is not competent to give legally valid informed consent to participate in research, such as a child or cognitively-impaired person. Failure to object to participation absent affirmative agreement does not qualify as assent.

CHILDREN Individuals who have not attained the legal age for consent to treatment or procedures involved in research according to applicable law of the jurisdiction in which the research will be conducted. In Maryland, individuals 18 years of age and older are of legal age (released from parental authority) and considered adults [http://mlis.state.md.us/cgi-win/web_statutes.exe - section 24]. (Also called **MINORS**.) There are several exceptions, such as marriage and childbearing, that can qualify individuals under the age of 18 as emancipated minors.

DECISIONALLY-IMPAIRED PARTICIPANT A participant whose capacity for judgment and reasoning is impaired and who therefore may be incapable of giving informed consent without a legally authorized representative (LAR).

EXCULPATORY LANGUAGE Words through which the prospective participant and/or the participant's legally authorized representative (LAR) is made to waive, or appear to waive, any of the participant's legal rights or is made to release, or appear to release, the investigator, the sponsor, the institution, or its agents from liability for negligence. Such language is not permitted in the informed consent process.

INFORMED CONSENT A process through which a person's voluntary agreement to participate in research is obtained after the person has been informed of the physical, psychological, and social risks and potential benefits posed by the study as well as the procedures involved [45 CFR 46.116]. Informed consent is usually demonstrated by signing a consent form, but it may be provided orally (under specific criteria approved by HIRB).

LEGALLY AUTHORIZED REPRESENTATIVE (LAR) An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to the participant's participation in the procedure(s) involved in the research.

WAIVER OF CONSENT Federal regulations permit IRBs to release investigators from or alter informed consent requirements in a limited number of circumstances, such as a medical emergency. The IRB also is permitted to waive documentation of informed consent under certain conditions.

8.1 Federal Regulations

Federal regulations require that legally effective informed consent be obtained from each research participant or his/her legally authorized representative (LAR) as follows:

1. Human participant research can proceed only with the consent of the individual or his/her LAR, unless waived in accordance with Federal regulations. Therefore, unless waived by HIRB, no investigator may involve a human being as a participant in research without the legally effective consent of that individual or his/her LAR.
 - Consent must be voluntary and given without undue influence. An investigator must seek consent under conditions that (a) minimize the possibility of coercion or undue influence and (b) provide the prospective participant or his/her LAR sufficient opportunity to consider whether to participate.
 - Consent must be in a language understandable to the participant or his/her LAR.
 - Waiver of a participant's rights is prohibited. Consent, whether oral or written, may not include any exculpatory language through which a prospective participant or his/her LAR is made to waive, or appear to waive, any of the participant's legal rights or is made to release, or appear to release, the investigator, the sponsor, the institution, or its agents from liability for negligence. (See Exculpatory Language in Section 9.4.)

8.2 Required Elements of Informed Consent

Federal regulations require that investigators provide specific information to potential participants and include certain additional elements when appropriate [45 CFR 46.116].

The required elements of informed consent are as follows:

1. A statement that the study involves research, an explanation of the purposes of the research, an estimation of the duration of the participant's participation, a description of the procedures to be followed, and identification of any procedures that are experimental.
 - A description of any reasonably foreseeable risks or discomforts to the participant.
 - A description of any benefits to the participant or to others that may reasonably be expected from the research.

- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant.
- A statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained.
- For research involving more than minimal risk, an explanation as to whether any compensation in the form of money or medical treatment is available if injury occurs and, if so, what it consists of or where further information about it can be obtained.
- A statement specifying whom to contact for answers to pertinent questions about the research and research participants' rights and whom to contact in the event of a research-related injury to the participant.
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled, and the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.

The following are additional elements of informed consent that may be required when appropriate:

1. A statement that the particular treatment or procedure may involve risks to the participant (and/or the embryo or fetus, if the participant is or may become pregnant) that are currently unforeseeable.
 - Anticipated circumstances under which the participant's participation may be terminated by the investigator without regard to the participant's consent.
 - Any additional costs to the participant that may result from participation in the research.
 - The consequences of a participant's decision to withdraw from the research and procedures for orderly termination of participation by the participant.
 - A statement that significant new findings developed during the course of the research that may affect the participant's willingness to continue participating in the study will be provided to the participant.
 - The approximate number of participants involved in the study.

Some studies may require further elements not listed above. For example:

1. Consent to establish a tissue or specimen repository.
 - Consent for possible commercial use of human tissues.

8.3 Waivers and Alteration of Informed Consent

With the important exception of FDA-regulated research (see below), HIRB has the authority to:

- Waive the requirement to obtain consent.
- Waive or alter some or all of the required elements of informed consent.
- Waive the requirement to obtain a signed written consent form for some or all participants.

HIRB may waive or alter some or all of the informed consent requirements under *either* of the two conditions below (also see Chart 9 in Appendix A):

1. The study is an investigation of public benefit or service programs, and HIRB finds and documents *all* of the following:
 - The research or demonstration project will be conducted by, or subject to, the approval of state or local government officials.
 - The research is designed to study, evaluate, or otherwise examine public benefit or service programs, procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs.
 - The research could not practically be carried out without the waiver or alteration.

Note: Public benefit programs are narrowly defined in the Federal regulations.

- The research is minimal risk, and HIRB finds and documents *all* of the following:
- The research involves no more than minimal risk to participants.
- The waiver or alteration will not adversely affect the rights or welfare of participants;
- The research could not practicably be carried out without the waiver or alteration.
- Participants will be provided with additional pertinent information after participation when appropriate.

HIRB may waive the requirement to obtain a signed consent form (i.e., waive documentation) from some or all participants if it finds and documents *either* of the two conditions below (also see Chart 10 in Appendix A):

1. The only record linking the participant to the research would be the consent document, and the principal risk of retaining this link would be a breach of confidentiality. In this case, each participant will be asked whether she or he wants documentation linking her or him to the research, and the participant's wishes will govern.
 - The research presents no more than minimal risk to participants and involves no procedures for which written consent is normally required outside of the research.

When consent is obtained without a signed document, HIRB may require that evidence of oral consent be included in each participant's record. HIRB also may require that an investigator give research participants a written statement about the research even though it has approved a waiver or alteration. Additionally, Federal, state, or local laws may require that certain information, such as the process for reporting certain communicable diseases, be disclosed to participants in order for consent to be legally effective.

Waivers for FDA-Regulated Studies

The FDA requires that investigators obtain informed consent from all participants unless the participant is facing a life-threatening situation that necessitates the use of a test article. Therefore, the informed consent process cannot be waived when identifiable human participants or specimens

are involved in FDA-regulated research. The FDA permits waiver of documentation of informed consent in studies involving minimal risk of harm and no procedures for which written consent is generally required outside of the research context.

Applying for Waivers and Alterations

To apply for a waiver or alteration of the informed consent requirements, investigators should submit an Informed Consent Requirements Waiver/Alteration form to HIRB with their application for approval of new research. To apply for a waiver of consent documentation, investigators should similarly submit an Informed Consent Documentation Waiver form. These forms are available on the HIRB Web site. Investigators must justify their request for waiver or alteration with respect to the Federal regulations. When HIRB approves a procedure that waives or alters the consent requirements or waives documentation, it will document that the study meets applicable Federal requirements. Waiving or altering informed consent requirements without HIRB approval constitutes a violation of Federal regulations and HIRB policy and procedures, as does waiving documentation without HIRB approval.

8.4 Emergency Waivers

Federal regulations also allow for a waiver of the requirement for obtaining and documenting consent for research participants who urgently require the intervention being studied but, because of their medical condition, are unable to give consent. One of the two procedures outlined below must be followed:

1. The intervention may be used provided that the investigator and an independent physician not connected with the study certify *both* of the following in writing:
 - The participant has a life-threatening condition that requires the intervention being studied, and informed consent cannot be obtained because the participant cannot communicate effectively.
 - Time is not sufficient to obtain consent from the participant's Legally Authorized Representative (LAR), and there is no recognized therapy that provides an equal or better chance of saving the participant's life.
 - If, in the investigator's opinion, the above conditions exist but documentation by an independent physician is not possible in the time available, the intervention may be used. The determinations of the investigator must then be reviewed and evaluated in writing by an independent physician within five working days.

In each of the above procedures, the documentation by the investigator and the independent physician must be provided to HIRB for review within five working days after the intervention has been used.

When emergency medical care is initiated without prior IRB review and approval, the individual may not be considered a research participant, the emergency care may not be claimed as research, and no data regarding such care may be included in any report of a prospectively conceived research activity. Investigators should contact the HIRB Office for additional information on waiver of the informed consent requirements in emergency situations.

8.5 Deception of Participants

Deception is the intentional withholding of information related to the research from participants or the intentional provision of false information to participants about some aspect of the research. Deception poses an ethical problem because it prevents individuals from being fully informed about the research prior to enrollment and participation. However, although some psychologists have overemphasized the value and necessity of its use, deception may be the only scientifically valid approach for some studies. For example, to discover whether certain kinds of background music are more distracting than others in a learning situation, an investigator might explain to participants that certain aspects of learning and memory are being studied without mentioning anything about background music and distractions. Participants would be told that they are required to learn sets of words and then tested on how well they remember those words. They would be deceived about the true purpose of the research and certain elements of the study design.

Studies involving deception pose psychological and social risks. Participants may be upset or embarrassed about being deceived and/or by how they acted or what they revealed about themselves during the deception. Some participants would not have agreed to participate had they known all the details about the study prior to enrollment. Investigators must minimize these risks, and the research benefits should offset them.

Deception is not allowed unless it is essential to the goals of the research and approved by HIRB. Investigators must obtain a waiver of some of the informed consent requirements from HIRB in order to use deception. When deception is involved, HIRB must be satisfied that the deception is necessary and the proposed population is appropriate for it. HIRB may require that investigators debrief deceived participants. In some cases, however, debriefing itself may present an unreasonable risk of harm without a countervailing benefit and should not be conducted. For instance, when the debriefing would reveal something potentially embarrassing or distressing to participants about their own attitudes or behaviors without offsetting benefits, HIRB generally will not endorse it.

8.6 Tests of Understanding

Prospective research participants have the right to be fully informed about the research in which they are asked to take part. Although investigators may carefully provide information about the study and individuals' rights as participants, prospective participants may not sufficiently comprehend the information to give fully informed consent, especially when the information is unfamiliar to them or technically complex. In such instances, especially when risk is greater than minimal, it may be important to confirm that understanding is adequate before a prospective participant accedes and signs the consent document.

Simply asking whether the participant understands is not always sufficient. Rather, understanding must sometimes be confirmed by asking specific questions about the research that the participant answers correctly. A test of understanding is a tool that can strengthen the consent process. For studies that are not technically complex, the test may be conducted orally using a standard set of questions. For studies that are complex or require comprehension of a large amount of information, a written test of understanding is usually better. A written test not only assures a uniform process for assessing understanding; it also provides a written record that becomes part of the participant's file. HIRB reviews tests of understanding as part of its review process.

Tests of understanding should be based on the required elements of informed consent and will usually include at least the following items:

- The purpose of study.
- Any treatment to be given (if relevant).
- Alternatives to participating (if relevant).
- The risks of participation.
- The benefits of participation.
- Provisions to ensure confidentiality.
- The right to withdraw from the study.
- Who, if anyone, will pay for study-related expenses (e.g., transportation, medical costs)?
- An opportunity for the participant to ask the researcher(s) questions.

A sample test of understanding is available from the HIRB Office upon request.

Oral Tests

Oral tests should be based on a written script to ensure that the same process is followed with each participant. Questions should be designed to determine whether participants understand key elements of the information that has been given to them. Questions that are answered by “yes” or “no” are less helpful because they provide no information about the participant’s level of understanding, and the participant may guess the correct answer. Simply asking a participant if she or he understands also provides little useful information. The participant is likely to answer affirmatively even when she or he does not understand. The best questions are those that are open-ended and ask “what,” “why,” “when,” “where,” or “how.” For example:

- Why were you asked to take part in this study?
- What will you be asked to do in this study?
- What will happen if you decide you no longer want to be in the study?
- Who should you contact if you have any questions?

When an answer is unclear, follow-up questions should be asked to determine whether the participant’s understanding is correct.

Written Tests

Written tests provide a permanent record of a participant’s understanding but are generally less flexible in format than oral tests, particularly because it is not easy to ask follow-up questions to confirm understanding. Written tests usually consist of multiple choice items, true/false questions, or short answer questions that can be answered in one or two words. Participants are required to answer correctly a predetermined percent of the questions, for example 75%.

Feedback and Failure to Pass Tests

A test of understanding, whether oral or written, provides an important opportunity to improve a participant's understanding of the planned research. This is done, for instance, by providing the correct answer and explaining why it is correct when a participant has answered a question incorrectly and by encouraging the participant to ask any questions that may have arisen while taking the test.

Investigators should describe in their research protocol what happens when a participant fails to pass an oral or written test. Because failure to pass may be due to poor test taking skills and/or anxiety, failure should not automatically exclude a participant from the study. Investigators may propose that a research team member further assess the participant's understanding after feedback has been provided. Investigators should determine at what point a participant must be excluded or requires the consent of a legally authorized representative (LAR) in order to enroll.

8.7 Participants Unable to Consent

Federal regulations stipulate that no investigator may involve a human being as a participant in research unless the investigator has obtained legally effective informed consent from the participant or the participant's legally authorized representative (LAR), unless a waiver has been granted by an IRB. Not all individuals have the capacity to provide legally informed consent on their own; for these individuals, proxy consent must be obtained. For research conducted in Maryland, the following classes of persons, in order of priority, are authorized under the Maryland Health Care Decisions Act of 1993 to provide consent for health care, and by extension consent to research, on behalf of a participant who is unable to consent for himself or herself and has not appointed a health care agent: (1) guardian; (2) spouse; (3) adult child; (4) parent; (5) adult sibling; and (6) friend or other relative, provided that person is competent and presents an affidavit to the investigator stating that (a) the person is a close friend or relative and (b) the person has maintained regular contact with the participant. HIRB Office staff can provide additional information concerning proxy consent.

8.8 Child Assent/Parental Permission

Federal regulations require that (1) to the extent that they are able, children be given the opportunity to agree (i.e., assent) or disagree to take part in research and (2) the permission of their parent(s) or guardian be obtained unless waiver requirements have been satisfied. All of the requirements concerning informed consent apply to parental permission (i.e., the required elements of informed consent must be included in parental permission forms). Templates for parental permission and assent forms are available on the HIRB Web site. The waiver options for informed consent also apply to parental permission.

HIRB requires that assent be obtained from children ages 7 years or older. The form and content of the assent depends on the age of the child. Younger children cannot provide assent, but they should be appropriately informed of study procedures to the extent possible.

Children younger than 7 years. A simple oral explanation should be offered to the child before study-related procedures are conducted unless the child is too young to understand such an explanation. For instance, for a study of cognitive development, the child may be told: "We are going to show you a video while you sit in your mom's [or other caregiver's] lap. After the video, we

will ask you some questions about what you saw.” The simple oral explanation should be included in the HIRB application.

Children 7 to 11 years. Informed voluntary verbal assent should be obtained from the child without pressure from parents or investigators. The HIRB application should include an example of the explanation to be offered to the child. A sample child assent form is available on the HIRB Web site. Assent from the child should be solicited and recorded in the presence of a parent, and the parental permission form should include a statement such as follows: “This study has been explained to my child in my presence, in language s/he can understand. S/he has been encouraged to ask questions both now and in the future about the research.”

Children 12 to 15 years. Investigators may choose to handle the consent/assent requirements for this group in one of two ways. They may submit either (1) a consent form that is written at a level simple enough for both the parent(s) and child to read and understand (e.g., about a 6th-grade reading level) or (2) a permission form for one or both parents to sign and a separate assent form for the child to sign. If a permission form is designed for both parent(s) and child, it should be signed by each of them after the study has been explained. The permission form should be written as simply as possible and should cover the following points:

- What the study is about.
- Why the child was selected for the study.
- That taking part in the study is voluntary.
- The procedures that will be performed.
- Potential benefits of the study.
- Potential risks of the study.
- Assurance that the child will be treated the same whether or not s/he agrees to participate in the study.
- An invitation to ask questions about the study.
- Assurance that the child may withdraw from the study after discussing withdrawal with her/his parents.

Children 16 to 18 years. A permission form written in language that is easily understandable to both the parent(s) and child is sufficient for this group. A separate assent form need not be used. The parent(s) and the child must sign the consent form.

Child Consent Without Parental Permission

Under certain conditions, children may be able to consent to research without parental permission. Investigators should consult state and local laws and regulations for exceptions to obtaining parental permission. If a waiver of parental permission is requested, a concise but complete justification must be provided to HIRB. The following is a list for Maryland of the most common research situations in which a child may be able to consent to participate in research without parental permission:

- The child is not living with and is financially independent from parent(s) and/or guardian.
- The child is pregnant, and the research and treatments concern her pregnancy.
- The child wants specific treatment or advice about drug abuse, alcoholism, sexually-transmitted diseases, pregnancy, or contraception (other than sterilization).
- The child is at least 16 years old, and the research consists of consultation, diagnosis, and/or treatment of a mental or emotional disorder by a physician, psychologist, or a clinic.
- The child is validly married or is a parent.

There are additional limited situations in which children may consent to participate without parental permission. The HIRB Office can provide further information if needed.

8.9 Decisionally-Impaired Adults

Individuals whose decision-making capacity is restricted, wholly or in part, due to illness, mental disability, or other circumstances may be incapable of making informed judgments about whether to enroll or continue participation in a study. The Common Rule requires that additional safeguards be in place to protect the rights and welfare of individuals who may be subject to undue coercion or undue influence, including mentally disabled persons. There are, however, no additional DHHS regulations that specifically concern protection of participants who are unable to make informed decisions due to cognitive impairment or another disability.

HIRB considers decisionally-impaired individuals to be vulnerable and in need of additional protections. It has developed the following policy based on NIH guidance entitled, *Research Involving Individuals with Questionable Capacity to Consent: Points to Consider*. The policy includes, but is not limited to, the following categories of studies:

- Psychiatric studies, where it is anticipated (but not presumed) that patients may be or become decisionally impaired.
- Clinical protocols involving medical conditions that often (but not always) render a person physically unconscious or decisionally impaired (e.g., stroke, unstable or serious cardiac conditions, shock, trauma, drug abuse, fever, infections, and other reversible conditions causing changes in mental status).
- All other research that may include participants who might experience fluctuating decisional capacity (due to dementia, emotional distress, illness, etc.).

Selecting Participants and Obtaining their Consent

It should not be assumed that incapacitated or decisionally-impaired participants are incapable of giving valid initial or ongoing consent. Investigators who will conduct studies in which the decision-making capacity of some or all participants may be impaired, either prior to enrollment or during the course of the study, should address the following points in their research plan.

1. The research should be conducted on participants who have the capacity to consent before being conducted on participants who are unable to give consent.

- The research protocol should describe procedures for assessing a participant's capacity to consent and the circumstances in which consent will be sought from a Legally Authorized Representative (LAR) recognized by the state in which the research will be conducted. Investigators should consider a two-part consent process when appropriate: (1) an assessment of comprehension and recall and (2) a test of understanding. Capacity should be determined in relation to the research tasks. For research protocols that present greater than minimal risk, HIRB may require that an independent, qualified professional assess the potential participant's capacity to consent. The protocol should describe who will conduct the assessment, the nature of the assessment, and the criteria for determining that an LAR is needed. HIRB will permit investigators to use less formal procedures to assess a potential participant's capacity if there are good reasons for doing so.
- When potential participants are capable of making informed decisions about participation, they may accept or decline participation without the involvement of any third parties. No person who has the capacity to consent may be enrolled in a study without his or her informed consent.
- A person who has been determined to lack capacity to consent to participate in a research study must be notified of that determination before permission may be sought from his or her LAR to enroll the individual in the study. Furthermore, if permission is given by an LAR to enroll a person in the study, the potential participant must be notified. Should the person object to participating, her or his objection must be respected.
- If a research participant has fluctuating or limited decision-making capacity or is likely to become incapacitated during the study, investigators should establish and maintain communication with involved caregivers, consistent with the participant's level of autonomy and the need for confidentiality.
- Any objection to enrollment or continued participation in a study by a potential or actual participant must be respected. An investigator, acting with a level of care and sensitivity that avoids the possibility or appearance of coercion, may approach people who previously declined to participate or decided not to continue in a study to ask whether they have changed their minds.
- Research protocols should include a thorough justification of the research design, including a description of the prospective benefits and procedures designed to minimize risks to participants. The evaluation of benefits should distinguish possible direct medical benefits to the participant from other types of benefits. Studies that elicit symptoms, withdraw participants rapidly from therapies, use placebos, or expose participants to greater than minimal risks must be thoroughly justified. Individuals who have been determined to lack capacity to consent should not be enrolled in research that is unlikely to result in direct benefit to them, unless the research presents no more than minimal risk.

8.10 Consent in Languages Other Than English

Federal regulations require that consent be obtained in a language understandable to participants. If non-English speaking participants will be included in a study, consent documents must be written in a language in which they are fluent. The English version of the consent document(s) must be submitted with the application for HIRB review and approval of new research. However, HIRB will not grant final approval until the English language consent documents have been translated into the potential participants' language and a Certificate of Translation has been obtained to validate the translation. Investigators conducting the research may not certify the translation. A translator who is fluent in English and the potential participants' language may certify the translation. For international research, a local IRB, Ethics Committee (EC), or government agency can certify the translation. Any changes in the consent documents that are required by the local IRB, EC, or government agency must be submitted to HIRB, along with a revised English version of the consent documents, for review and final approval. Contact with participants may not be initiated until HIRB has formally approved both the English and non-English versions of the consent forms and has received the Certificate of Translation.

Unless HIRB has authorized use of the alternative short consent form (see Section 9.1), informed consent should be obtained with a document in the local language that contains all of the basic elements of informed consent and appropriate additional elements. Under the alternative short-form procedure, oral presentation of consent information may be provided together with a short consent form, both in a language understandable to potential participants. A summary document including all required informed consent elements should be prepared in English. The regular English informed consent form can serve as the summary document. A witness who is fluent in both English and the participant's language must observe the informed consent process. If a translator assists the person obtaining consent, the translator can serve as the witness. The participant or the participant's legally authorized representative (LAR) should sign the short consent form, the investigator obtaining consent should sign the written summary, and the witness should sign the short consent form and the written summary. The participant or LAR should receive a copy of the short consent form and the written summary. HIRB must review the non-English version of the short informed consent form as well as the non-English script for the oral summary and the English written summary. Expedited review of these documents is permitted if the research protocol, the regular English informed consent document, and the English version of the short informed consent form have already been approved by HIRB.

8.11 Consent via Phone

Federal regulations require that informed consent be documented by a written consent form that has been approved by HIRB and signed by the participant or the participant's legally authorized representative (LAR), unless HIRB has waived such documentation. Studies involving surveys or interviews conducted over the telephone are no exception to this requirement. Written consent to take part in a survey or interview may be obtained prior to contact by telephone. Alternatively, HIRB may waive the requirement for obtaining a signed consent under *either* of the two conditions listed below:

1. The study is no more than minimal risk, the only record linking the participant and the research would be the consent document, and the primary risk would be potential harm resulting from a breach of confidentiality.

- The study is no more than minimal risk and involves no procedures for which consent would normally be required.

Requests for waivers must be included in the HIRB application for review of new research.

8.12 Secondary Research Participants

Researchers may seek to obtain private information from participants about other individuals. For instance, in a study of genetics, an investigator might request information from participants about the physical or mental health of family members. The family members may be considered secondary research participants, and their consent may be required before the individual is asked to provide information about them. When private information is obtained from a participant about another individual and that person is identifiable, the individual is a secondary research participant. On the other hand, when private information is obtained from a participant about another individual and that individual's identity is not revealed or the information would not place the individual at risk if disclosed, the individual is not a secondary research participant.

- If a participant is asked, "Does anyone in your family experience depression?," private information is ***not*** being collected about an identifiable individual and the individual would not be considered a secondary research participant.
- If a participant is asked, "Does your mother experience depression?," private information about an identifiable individual is being collected and the individual (the mother) would be considered a secondary research participant.

Investigators may need to obtain informed consent from secondary participants. If the information to be collected from primary participants about secondary participants is identifiable and the research is more than minimal risk, written informed consent from secondary participants is needed, unless HIRB waives consent from secondary participants prior to collection from primary participants. (See Charts 11 & 12 in Appendix A.)

Note: These are provisional guidelines. OHRP has not yet issued formal guidance on consent requirements for secondary research participants.

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Section Nine: Consent Documents
Date of Revision: 11/16/14

Introduction

Informed consent documents are a critical component of the informed consent process. Indeed, Federal regulations require that participants provide written consent except under limited circumstances in which the IRB is permitted to waive documentation (see Section 8.3). In many cases when documentation is waived, investigators are required obtain consent orally. The Homewood Institutional Review Board (HIRB) reviews and must approve the content of consent forms, as well as scripts used to obtain consent orally, unless the requirements for informed consent are waived. Investigators are advised to compose their consent documents carefully according to instructions provided in this section. HIRB has also developed templates, which are available on the HIRB Web site, to assist investigators in preparing consent documents.

Section Objective

This section contains guidelines and suggestions for preparing written consent documents and description of HIRB's review and approval procedures for consent documents.

Relevant Definitions

BENEFIT Something that is useful to or improves the well-being of a participant or other individuals, such as treatment for a problem. Benefits can be direct or indirect. For instance, a direct benefit could improve participants' condition while an indirect benefit might improve scientific understanding of the condition but not directly alter it.

COMPENSATION (1) Money or gifts given to participants for participation in research. (Also referred to as **PAYMENT**.) Consent forms should not describe payment as a benefit of participation. (2) Money or medical treatment provided to participants injured by the research.

EXCULPATORY LANGUAGE Words through which the prospective participant and/or the participant's legally authorized representative (LAR) is made to waive, or appear to waive, any of the participant's legal rights or is made to release, or appear to release, the investigator, the sponsor, the institution, or its agents from liability for negligence. Such language is not permitted in informed consent documents.

INFORMED CONSENT A process through which a person's voluntary agreement to participate in research is obtained after the person has been informed of the physical, psychological, and social risks and potential benefits posed by the study as well as the procedures involved [45 CFR 46.116]. Informed consent is usually demonstrated by signing a consent form, but it may be provided orally (under specific criteria approved by HIRB).

LEGALLY AUTHORIZED REPRESENTATIVE (LAR) An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to the participant's participation in the procedure(s) involved in the research [45 CFR 46.102].

MINIMAL RISK When the probability and magnitude of anticipated physical or psychological harm or discomfort in the proposed research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests [45 CFR 46.102]. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of a routine physical examination.

RISK The possibility of harm or injury (physical, psychological, or social) resulting from participation in a research study. The likelihood and magnitude of possible harm varies from minimal to significant. Federal regulations define only one level of risk — minimal.

9.1 Regular and Short Consent Forms

Consent must be documented with a consent form that has been formally approved by HIRB, unless HIRB grants a waiver or alteration of this requirement. The consent form in most cases will consist of a document that includes all of the basic elements of informed consent and, when appropriate, additional elements. The participant or the participant's legally authorized representative (LAR) must sign this document.

Under special circumstances, such as when participants are illiterate, HIRB will allow a short consent form to be substituted for the regular consent form. The short consent form must state that all of the required elements of informed consent have been presented orally to the participant or the participant's LAR. In addition to the short consent form, a written summary or script of what will be said to the participant is required for HIRB review. The summary should include all of the required elements of informed consent (see Section 8.2) and be similar in content or identical to a regular consent form. In other words, investigators can prepare the regular consent form and use it as a script to be read to participants. The participant or LAR must sign the short consent form, a witness who is not the person obtaining consent must sign both the short form and the written summary, and the person obtaining the consent must sign the written summary.

Depending upon which consent form option approved by HIRB, participants must receive a copy of the regular consent form OR the short consent form and written summary. All signed consent documents must be retained on file by the PI. When appropriate, such as in clinical trials, the consent documents should be placed in participant patients' medical records.

9.2 Guidelines for Consent Forms

Investigators are advised to include the paragraph headings listed below in their regular consent forms. Suggested language is provided under some headings. In addition, an Informed Consent Template is available on the HIRB Web site.

Title of Research Project

Provide the following information: (1) the title of the project, (2) the PI's name and JHU affiliation, and (3) the date the form was prepared.

Purpose of Research Study

Explain (1) the purpose of the research project, (2) the goal of the study, and (3) why the study is important.

Explain why and how the participant was selected for the study and inform him/her why he/she is being asked to participate in the study. For example:

- “You are being asked to be in this study because you are an injection drug user at risk of HIV infection.”

Indicate how many total participants will be included in the study. If it is a multi-site study, state how many participants will be enrolled at the potential participant’s site and how many will be enrolled at all sites in total.

Procedures

Explain who is eligible for study and who is not (i.e., the inclusion and exclusion criteria). This may have been covered with the participant during the recruitment process but should be reiterated here.

If the study involves different treatment groups, explain how the treatments or interventions will be assigned. If treatment assignments are randomly determined, this process should be explained to participants. For example:

- “Treatment assignments will be made by drawing a card or number or by flipping a coin.”

State which, if any, procedures are experimental, are innovative, or will be done solely for research purposes.

State the procedures to be followed. It is often helpful to provide participants with a visit-by-visit list of what to expect while enrolled. For example:

- “At the first visit, you will be asked to complete several surveys on the computer.”

If the study involves a survey, describe the type of information to be collected; specify if the questions are personal or of a sensitive nature (e.g., related to personal finances, psychological or emotional experiences, sexual habits, marital or family situations, domestic violence, alcohol or illegal drug use).

Note: If participants are asked to provide personal, identifiable information about a family member, informed consent from that family member may be needed. (See HIRB’s policy on Secondary Participants in Section 8.11 for additional information.)

For studies involving clinical procedures, briefly explain them. Describe the examinations and tests in which participants will be involved. For instance:

- For blood draws, specify the number of times blood will be drawn and the amount to be drawn in household measures such as a teaspoon, cup, etc. For multiple blood draws, indicate the total amount to be drawn, such as 1 pint or 2 cups, and compare it to the amount routinely taken from blood donors.

Specify the approximate total duration of time participants will spend participating in the study, the approximate time required of participants for each of the main procedures and phases of the study, and any plans to contact participants for possible follow-up studies.

If there are plans to keep participants' names and addresses on file to facilitate recruitment for future studies (other than follow-up to the current study), inform participants of these plans and allow them to choose not to be notified about studies in the future if that is their wish.

If the study requires review of participants' medical records, participants must provide either a completed HIPAA authorization (for domestic studies) or a Medical Records Release Form (for international studies). This requirement should be stated in the consent form.

Risks/Discomforts

Describe all major and minor risks and their anticipated frequency. As appropriate, include:

- Physical risks, such as side effects of an intervention under study, physical discomfort during an examination, and exposure to radiation.
- Psychological risks, such as disclosure of embarrassing or upsetting information (e.g., diagnosis of mental illness, diagnosis of a learning disabilities, HIV test results).
- Social risks, such as disclosure of sensitive personal information (e.g., sexual behaviors) and information about illegal activities (e.g., illicit drug use) to those outside study.

Describe other study-related burdens and inconveniences, such as the time needed for participation.

If the study includes medical interventions, blood draws, or exposure to radiation and participants should not participate in other studies while enrolled, state this and provide the rationale (e.g., risk of intervention interactions, risk to the integrity of the study, etc.).

If appropriate, indicate that the intervention or procedure may involve currently unforeseeable physical risks to the participant (and/or embryo or fetus if the participant is or may become pregnant). This is generally not necessary for minimal risk studies.

Benefits

State the potential benefits of participation to participants. Do not overstate benefits; be realistic. Examples of potential benefits to participants include the opportunity to discuss issues under investigation, access to personal medical information generated by the study, and access to an intervention under study that may have a direct medical benefit to physical or psychological health.

If participants will not benefit directly from participation, clearly state this. For example:

- “There are no direct benefits to you from participating in this study.”

State the possible benefits to individuals with similar conditions or in similar situations. For example:

- “This study may benefit other people in similar situations by [explain how].”

State the possible general benefit to science or the population at large, if applicable. For example, in the case of general benefits accruing from advances in knowledge about the topic under investigation, a statement such as the following might be included:

- “This study may benefit society if the results improve understanding of [specify topic].”

Voluntary Participation and Right to Withdraw

Explain that participation in the study is entirely voluntary. Suggested language:

- “Your participation in this research project is completely voluntary. You have the right to withdraw from the study at any time.”

If relevant, explain that not joining the study, or withdrawing from the study at any time, will not jeopardize employment for those employed by an institution associated with the study or jeopardize currently available medical care for those who receive care at an institution associated with the study. Suggested language:

- “If you decide not to be in the study, or if you drop out of the study, your decision will not affect your job at [Name of Employer].” “If you decide not to be in the study, or if you drop out of the study, you will still get the same medical care at [Name of Institution/Clinic].”

Remind participants who are asked to complete surveys or interviews that they can refuse to answer any particular questions asked and can stop the interview at any time.

Investigators may request that participants who want to withdraw complete a final assessment. In these cases, make participants aware that completion of the final assessment is voluntary.

Circumstances that Could Lead Us to End Your Participation

Include this section if there are specific circumstances that could lead to the participant being taken out of the study (e.g., if the study is cancelled by the sponsor, enrollment is no longer in the best interest of participants, it may be unsafe for participants to continue, or participants fail to follow study procedures). This can be explained to participants as follows:

- “Under certain circumstances, we may decide to end your participation before you have completed the study. Specifically, we may stop your participation if [describe situations in which participant’s participation would be terminated].”

If pregnancy is an exclusion criterion for enrollment, describe what will happen if participants become pregnant while enrolled.

If the list of reasons for termination is not exhaustive, add a sentence such as follows:

- “There may also be other circumstances that would lead us to end your participation.”

If appropriate, explain how termination will affect payment. For example:

- “If we end your participation before you have completed the study, we will provide compensation for your participation up to that time.”

Alternatives to Participation

Explain realistic alternatives to participation; specifically, state what treatment will be offered or recommended to individuals who decline to participate. For instance:

- “The tutoring program provided in this study is not available anywhere else, but you can find similar tutoring programs outside the study.”

Note: This section may be omitted for observational studies, intervention studies on healthy participants, and when an alternative treatment or service is not available outside the research.

Confidentiality

Describe the procedures for protecting the confidentiality of the information collected from participants. For most studies, the following statement is appropriate:

- Any study records that identify you will be kept confidential to the extent possible by law. The records from your participation may be reviewed by people responsible for making sure that research is done properly, including members of the Johns Hopkins University Homewood Institutional Review Board (HIRB) and officials from government agencies such as the National Institutes of Health and the Office for Human Research Protections. All of these people are required to keep your identity confidential. Otherwise, records that identify you will be available only to people working on the study, unless you give permission for other people to see the records.

It is recommended that the following language be included in all consent forms, except where participants are strictly anonymous (i.e., names or any other personal identifiers are not collected):

- “Every effort will be made to protect the confidentiality of the information provided insofar as it is legally possible.”

Describe how the study records will be created, stored, and maintained to protect confidential information. Explain how participants will be identified in the creation of study records (e.g., use of code numbers rather than participants’ names on data sheets). Indicate how data will be stored (e.g., in a locked file drawer or in a password protected computer) and how long identifying data will be maintained (e.g., until completion of follow-up data collection or until study data have been analyzed and reported). For audiotapes and videotapes, indicate how and when they will be destroyed and how confidentiality will be protected in transcribed information (e.g., all names will be removed from the transcript).

Some studies may require disclosure of information to other parties. For such studies, explain what information will (or may) be disclosed and to whom. If relevant, participants need to be informed that certain communicable diseases, evidence of child or elder abuse, and/or evidence that the participant may harm himself/herself or others will be reported to appropriate authorities as required by law. Participants must be informed what information, if any, will be reported by name. (See Reportable Diseases and Conditions in Section 3.6.)

If there is reason to suspect that the data may be of interest in a legal proceeding, references to what is “legally possible” should be amplified. If a Certificate of Confidentiality has been issued to protect the data from subpoena, include this information in the consent form. (See Certificate of Confidentiality in Section 3.5.)

Costs

Describe any financial costs to participants, such as the cost of transportation to the study site, and whether participants will be reimbursed for these expenses.

Describe any financial costs for which the participant or the participant's health care insurer will be responsible as a result of enrollment. In some cases, health care insurers refuse to cover costs related to enrollment in an experimental clinical trial.

Note: If there are no costs to participants, this section does not need to be included.

Compensation

If participants are compensated financially or otherwise (e.g., extra credit in a course, a small gift, transportation reimbursement) for their participation, the compensation must not be coercive in amount or the way in which it is distributed. (See Payments to Research Participants in Section 10.5.) Payment is considered an incentive; it is not a benefit. Outline the amount, schedule, and procedures for any payments. If payments will be prorated, this should be explained. Any bonus for study completion should be listed. For example:

- “If you satisfactorily complete the study, you will receive \$000.00 to compensate you for your participation. \$000.00 of this amount is a bonus for completing all of the sessions. If you end your participation before completing the study, you will be paid for your participation up to that time, at a rate of \$000.00 per session. Payments are made by check at the end of the study.”

If relevant, describe free medical tests that will be performed. The provision of free medical care, including psychological screening and treatment, also can be included as an incentive but should not be listed as a benefit.

If no compensation is provided, include the following statement:

- “You will not receive any payment or other compensation for participating in this study.”

If You Have Questions or Concerns

Questions about the research. List the name and telephone number of the person in charge of the study. For international studies, a name and phone number of a local contact should be included. Suggested language:

- “You can ask questions about this research study now or at any time during the study, by talking to the researcher(s) working with you. You can also ask the person in charge of this study, [name of PI], any questions you may have about this study. You can ask him/her questions in the future if you do not understand something about the study.”

Questions regarding individuals' rights as research participants. List the name and telephone number of HIRB and, if applicable, other local oversight bodies. For international studies, list the name and phone number of the local IRB or a similar agency as well as HIRB and its number. Suggested language:

- “If you want to talk to someone about this research study because you feel you have not been treated fairly or have been hurt by being in the study, you should call the person in charge of this study, [name of PI], at [phone number], or call the Johns Hopkins University Homewood Institutional Review Board (HIRB) at (410) 516-6580. The person in charge of the study or the people in the HIRB Office will answer your

questions.” If relevant, you may add: “and/or help you to find medical care if you are hurt during the study.”

If You Are Harmed by Participating in the Study

Begin with the following statement, inserting the name, role, and phone number of the principal investigator or other appropriate contact:

- If you feel that you have been harmed in any way by participating in this study, please call [name and role] at [phone number]. Please also notify the Johns Hopkins University Homewood Institutional Review Board (HIRB) at (410) 516-6580.

Whenever a project involves a procedure that may result in an injury to participants, prospective participants should be advised as to the availability or unavailability of medical treatment or compensation and who will be responsible for the costs. Injury is not limited to physical harm. Investigators should also consider psychological, social, legal, and financial harm. If no compensation or treatment is available, include a statement such as follows:

- “This study does not have any program for compensating or treating you for harm you may suffer as a result of your participation.”

Note: Minimal risk studies do not need to include this section.

Sharing of New Findings

Explain that any new findings that emerge during the course of the study that might affect participants’ willingness to remain in the study, such as a new treatment for the participants’ condition, will be shared immediately with them. For example:

- “The investigators will share with you any new findings that might benefit you that may develop while you are participating in this study.”

Note: If the study is greater than minimal risk, HIRB may require inclusion of this section; otherwise, it typically is not included.

9.3 Tips for Writing Consent Forms

Although informed consent is a process, not just a form, the form is an important component of informed consent and must contain information in a language and format that is understandable to potential participants in order to enable them to make an informed decision about whether to enroll in the study and, if the decision is made to enroll, to document that decision.

Format, Style, and Reading Level

Consent forms must be typed. If continuation pages are necessary, plain sheets of paper may be used, as long as they are clearly numbered and the following information is typed at the top of each page: the title of the project, the name of the PI, and the date of HIRB approval of that version of the consent form. In the interest of simplicity, separate consent forms should be used for adult consent, parental permission for a child, child assent, etc.

Federal regulations require that the information presented in consent forms be conveyed in a language understandable to potential participants or their legally authorized representatives (LARs). Literate potential participants should be able to read and comprehend the forms. To meet this

requirement, HIRB has adopted the National Adult Literacy Study's (NALS) estimate of the average reading level as a target for most consent forms. In 1993, NALS reported that approximately one-half of the American population is functionally illiterate or has marginal literacy skills. NALS estimates that the average American reads at or below the 8th-grade level. NALS also found that people are reluctant to admit that they have difficulty reading. HIRB requires that consent documents be written at no more than an 8th-grade reading level and lower when appropriate for the population being studied. Investigators are advised to search the help section of their word processor to find information about the use of readability statistics.

The description of the study should be written as if the investigator were speaking to the participant. Use of the first person should be avoided; the second or third person is preferred.

Consent Information Investigators Often Overlook

Investigators often fail to include certain information, which is specified below, in their consent forms. Some of this information is specifically covered elsewhere in this manual but repeated here because investigators frequently overlook it. Investigators should include the following, if applicable:

- ***Faculty affiliation.*** State the affiliation of faculty involved in the study (e.g., the Johns Hopkins University Whiting School of Engineering). For international studies, add that Johns Hopkins University is in the United States. Also provide the affiliation of any non-JHU investigators.
- ***Sensitive questions.*** If sensitive questions will be asked, specify the general topics to be covered (e.g., sexual behaviors, alcohol/drug use, domestic violence).
- ***Urine tests.*** If urine will be tested, state the purpose of test (e.g., to detect drug use).
- ***Length of interaction.*** If an interview or survey is included, state the length of time the interview or survey is expected to last. For example, "We would like to ask you some questions about your health. This will take about 15 or 20 minutes."
- ***Data handling.*** Include information on how data will be stored (e.g., in locked file cabinets, in a password-protected computer), how long data will remain linked to participant identifiers (e.g., only until data collection has been completed), and if and when data will be destroyed (e.g., when the study is completed and reported, after five years, etc.).
- ***Access to data.*** Provide a statement describing who may have access to participants' data.
- ***Payment is not a benefit.*** Do not list compensation for time and inconvenience as a benefit of participation; list payment under a separate heading as "Compensation."
- ***Reasons for termination.*** State the circumstances (if any) that could cause investigators to end participants' participation in the study.
- ***Pregnancy provisions.*** If pregnancy is an exclusion criterion for enrollment, include a statement explaining what will happen if the participant becomes pregnant while enrolled.

- **Local contact.** For international studies, provide the name and phone number of a local contact for participants.

Improving Understanding

The following steps are recommended to improve participants' understanding of consent forms.

1. Lower the reading level. Use simple language whenever possible and short, simple sentences of varied length. Avoid polysyllabic words (e.g., “take part in” instead of “participate”; “needed” instead of “clinically indicated”).
 - The following Web site offers replacement words and phrases for polysyllabic terms frequently used in consent forms, as well as instructions for assessing readability: [www.cdc.gov/od/ads/smog.html].
 - Know the targeted audience in order to gauge its reading level and understanding of technical terminology.
 - Limit medical terms and explain those that are used. Information on the following Web sites might be helpful:
 - Glossary of Medical Lay Terms [<http://ovcr.ucdavis.edu/HumanParticipants/HSDefinitions/HSGlossary.cfm>].
 - Glossary of Plain Non-Medical Language [<http://www.plainlanguage.gov/library/smpl1.htm>].
 - Avoid legal terminology.
 - Be consistent with terminology and define technical words if they cannot be replaced with simpler ones.
 - Describe the procedures in a logical, organized manner.
 - Use visual aids, charts, diagrams or pictures to describe complicated or detailed procedures.
 - Use at least a 12-point font (consider using a larger font based upon the targeted audience).
 - Use a 50/50 blend of white space in documents and charts.
 - Use headers to display new information.
 - Use interactive techniques, such as leaving a space for questions.
 - Test the consent form with the targeted audience.

9.4 Exculpatory Language

No informed consent, whether oral or written, may include any exculpatory language that releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence or through which the participant or the participant's LAR is made to waive or appear to waive any of the participant's legal rights.

Examples of unacceptable exculpatory language:

- “I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.”
- “By agreeing to this use, you should understand that you will give up all claims to personal benefit from commercial or other use of these substances.”
- “I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. Government and hereby relinquish all rights, title, and interest to said items.”
- “By consenting to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.”

Examples of acceptable language:

- “This hospital (or the appropriate JHU Homewood Division) is not able to offer financial compensation nor to absorb the costs of medical treatment should you be injured as a result of participating in this research.”
- “This hospital (or the appropriate JHU Homewood Division) makes no commitment to provide free medical care or payment for any unfavorable outcomes resulting from participation in this research. Medical services will be offered at the usual charge.”
- “Tissue obtained from you in this research may be used to establish a cell line that could be patented and licensed. We will not compensate you financially should this occur.”
- “By consenting to participate, you authorize the use of your bodily fluids and tissue samples for the research described above.”

9.5 Review and Approval of Consent Forms

Consent forms must be approved and stamped (i.e., validated) by HIRB before being used in the informed consent process. When HIRB is the only IRB for a study, its approval is indicated by a stamp on the consent forms. When other IRBs are involved, HIRB and the other IRB(s) must approve the forms that will be used in the consent process. This usually involves initial review and approval by HIRB. The consent forms are then stamped by HIRB and sent to the local IRB(s) for review. If the local IRB(s) request substantive revisions, these must also be approved by HIRB. After HIRB and the local IRB(s) agree on the content and format of the consent forms, the forms are stamped by HIRB and can be used in the consent process. For statistical and coordinating centers, HIRB can delegate final approval of consent forms that will be used at individual study sites to each respective local IRB.

When consent will be obtained in a language other than English, investigators must arrange for the translation of the consent forms into a language that potential participants can understand. The translation must be completed by someone not on the study team and may take place before or after initial review by HIRB. However, it is recommended that investigators first submit an English language version of their consent forms to HIRB for approval. If HIRB requires revisions, investigators can make them before the documents are translated, eliminating the need for multiple translations. A Certificate of Translation signed by the translator must be provided to HIRB to attest to the accuracy of the translation of the HIRB-approved English language consent forms. HIRB

may, if it wishes, obtain a back translation of the non-English language forms to confirm their accuracy. Once HIRB is satisfied, it stamps the non-English language forms to attest that they may be used in the consent process.

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Section Ten: Participant Recruitment & Compensation
Date of Revision: 11/16/14

Introduction

The ethical principles of respect, beneficence, and justice apply to the treatment of human research participants throughout the entire research process, including the recruitment phase. In recruiting participants, investigators must respect potential participants and not mislead or coerce them into enrolling in a study. Investigators also must not take advantage of certain populations of participants, such as employees and students, because they are more easily accessed and persuaded to enroll. In addition, payments to participants must not unduly influence participants' enrollment decisions. Potential participants also must be informed what compensation, if any, they will receive if injured by the study.

The Homewood Institutional Review Board (HIRB) reviews all recruitment plans and materials. Recruitment may not commence until HIRB approval of the research protocol has been granted. HIRB also evaluates the appropriateness of payments and compensation for injury, if any, and how participants are informed of each.

Section Objective

This section contains guidelines regarding recruitment materials; the recruitment of specific populations, namely minorities, women, employees, and students; payments to participants; and compensation for injury.

Relevant Definitions

COMPENSATION (1) Money or gifts given to participants for participation in research. (Also referred to as **PAYMENT**.) Consent forms should not describe payment as a benefit of participation. (2) Money or medical treatment provided to participants injured by the research.

DIRECT ADVERTISING Written scripts, mailings, printed flyers, posters, newspaper advertisements, press releases, television and radio spots, videotapes, web pages and electronic mailings that are intended to be seen or heard by prospective participants to solicit their participation in a study.

PAYMENT Money or gifts given to participants for participation in research. Consent forms should not describe payment as a benefit of participation. (Also referred to as **COMPENSATION**.)

10.1 Recruitment Materials

The use of direct advertisements to recruit potential research participants often begins the process of participant selection and informed consent. Direct advertisements are intended to be seen or heard by prospective participants in order to solicit their participation in a study. Direct advertisements include, but are not limited to, written scripts, mailings, printed flyers, posters,

newspaper advertisements, press releases, television and radio spots, videotapes, web pages, and electronic mailings.

Applications for new studies submitted to HIRB for review must describe in detail the content of all advertisements, as well as when, where, and how the advertisements will be communicated to potential research participants. The advertisements should accurately describe the purpose of the study and study procedures. For example, if the study will involve a control group, the advertisement should state that some participants will be assigned to a control group. Additionally, the advertisement should not falsely imply or suggest that the research is an opportunity for free medical treatment. Overall, the advertisement should be limited to the information that prospective participants need in order to determine their eligibility and interest in enrolling.

All advertisements must be approved by HIRB before being used to recruit participants. If developed after HIRB initially approves the study, they must be submitted for approval through an Application for Amendments and Changes. HIRB will review the information contained in the advertisement as well as the mode of communication. HIRB pays special attention to advertisements when the study will involve persons with acute or severe physical or mental illness, children, individuals who are economically or educationally disadvantaged, or members of other vulnerable populations. The goal of the HIRB review is to ensure that recruitment procedures are informative without being coercive or misleading or implying an outcome or benefit to participants that is not described in the study protocol and consent documents.

The content of advertisements should be limited to the following:

- The name and address of the PI.
- A statement that the study is being conducted by the division in which the PI has his or her primary appointment.
- A statement that the study is research.
- Where the research will take place.
- The purpose of the study.
- A brief description of study procedures.
- A brief description of the eligibility criteria.
- A straightforward, truthful description of any benefits to participants.
- A straightforward, truthful description of any incentives for participants. (The amount of payment may be stated but should not be stressed; alternatively, the advertisement may simply state, “A payment will be provided.”)
- The time commitment required of participants.
- The person to contact for further information and how to contact him or her.

The advertisement should avoid *all* of the following:

- Statements that may be considered coercive.

- Misleading statements about benefits from participating in the study.
- Promises of “free medical treatment,” when the intent is to say that participants will not be charged for taking part in the investigation.
- Suggestions that the safety or effectiveness of an investigational drug, biologic, or device has been determined to be equivalent or in any way superior to any other drug or device.
- Use of the name of a commercial sponsor or product manufacturer.
- Statements that directly communicate or imply that the certainty of a favorable outcome or other benefit is beyond what is outlined in the consent documents and research protocol.
- Overemphasis on payment as an enticement to enroll (e.g., indicating the amount of payment in a larger font than other text or in bold or brightly colored type).

The wording of all advertisements must remain exactly as approved by HIRB. The PI is required to maintain an approved copy of recruitment materials, which will contain the HIRB stamp, study number, and approval and expiration dates. HIRB approval of advertisements is only valid for the period for which the study is approved, which cannot exceed one year. Review and renewed approval of advertisements is required with each continuing review of the study unless advertisements are no longer in use.

10.2 Recruitment of Minorities and Women

Investigators and IRBs are responsible for ensuring the equitable selection of participants in research. *The Belmont Report* emphasizes the importance of including men, women, and minorities in research so each group can share equally in its benefits and no group bears a disproportionate share of its burdens. The report also stresses that investigators should include the broadest range of population groups in their research to enable results to be generalized as widely as possible.

In 1994, NIH established guidelines on the inclusion of women and minorities in the biomedical and behavioral research that it funds. In 2001, NIH updated these guidelines, which state:

- “It is the policy of NIH that women and members of minority groups and their subpopulations must be included in all NIH-funded clinical research, unless a clear and compelling rationale and justification establishes to the satisfaction of the relevant Institute/Center Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research.”

This policy further stipulates that cost is not an acceptable reason for excluding a particular group or subgroup. It also specifically prohibits the exclusion of women of childbearing age from research without reasonable scientific justification. Although DHHS previously stipulated that paternal consent was required for a pregnant woman to participate in research, this is no longer always the case. The Clinton Administration’s January 17, 2001, changes to the Common Rule [45 CFR 46] made a pregnant woman the sole decision-maker about whether to participate in research under certain conditions. (For more details, see Section 11.2.)

Proposals for NIH-supported research, including exempt research, must include details on the selection of research participants, including characteristics of the populations from which participants will be drawn, anticipated numbers of participants from each population, their age

range, and health status. The gender and racial/ethnic composition of the sample and populations from which they are drawn must also be described, as well as the rationale for including or excluding any specific groups.

HIRB uses the NIH requirements as a general guide when reviewing research, regardless of the funding source. More specifically, HIRB considers *all* of the following when reviewing applications for new studies:

- The sex, race, ethnicity, and age of the targeted study sample.
- The characteristics of the larger populations from which study participants will be recruited.
- Whether the study sample is appropriate for the purpose of the research.
- The inclusion and exclusion criteria and the rationale for them.
- Whether any groups or individuals will be excluded from the research without good scientific justification.

At the time of continuing review, investigators must provide specific information on the enrolled sample. The board may, based on the information provided, require investigators to explain why a specific group has not been enrolled or is over- or underrepresented.

10.3 Recruitment of JHU Students

Ethical concerns arise when JHU students are recruited as participants for Homewood research studies. These concerns relate primarily to possible undue pressure to enroll and potential breaches of confidentiality. In 2005, the JHU Council of Deans approved a policy governing the recruitment and enrollment of JHU students in JHU research. A student is defined by the *Johns Hopkins University Policy Concerning the Recruitment and Enrollment of Students in Research Involving Human Subjects* as, “an individual who has registered within any academic division of Johns Hopkins University, regardless of whether s/he is enrolled in courses or on authorized leave.” The policy defines educational research as, “scholarly inquiry with the ultimate goal of improving the educational process or learning environment.”

Recruitment

An investigator, whether faculty member, student, or staff member, may not directly solicit participation in his or her research project from any JHU student whom the investigator teaches or supervises in an academic capacity, regardless of the study’s level of risk. This prohibition applies even if the student has previously indicated willingness to be contacted about the possibility of participating in research, for instance, by placing her name in a research pool. There is one exception to this policy. For minimal risk educational research, HIRB may waive the prohibition against faculty recruitment of their own students based on the burden, risk, and extent of departure from standard educational practice that the proposed research involves and the need for the exception.

JHU students may be recruited through indirect methods such as the posting of HIRB-approved flyers and the placement of HIRB-approved advertisements. Students who submit their names to a research pool may be contacted directly by phone or e-mail if neither the recruiter nor the investigator supervises them academically.

Research involving JHU students who are under 18 years of age is subject to the same regulations and guidance as all research involving children (see Section 7.8). Investigators have the responsibility of ensuring that any potential participants who are children are identified and their enrollment complies with these regulations.

Participation Incentives

The use of monetary incentives for soliciting the participation of JHU students is permissible but must be guided by the same considerations and constraints as the use of such incentives for all human participants (see Section 6.4).

The use of extra credit as an incentive for JHU students to participate in research is acceptable if such participation offers educational benefits to the students in question and the students are offered nonresearch alternatives by which they may earn an equivalent amount of extra credit. Appropriate nonresearch alternatives may include such activities as attending a departmental seminar or event, watching an educational film, or writing an essay. Alternatives must not entail more time, effort, or stress on the part of the student than the research activity (e.g., writing a five-page essay is not proportional to the task of filling out a two-page survey). Academic departments may place additional restrictions on the use of extra credits as an incentive to participation.

Minimal Risk Research

JHU students are permitted to enroll in studies that qualify as minimal risk. While investigators are not allowed to directly recruit students whom they teach or supervise, they may enroll students as research participants should the students respond to indirect recruitment methods. For minimal risk educational research, HIRB may waive the requirement for informed consent or the prohibition against faculty members' recruitment of their own students based on the burden, risk, and extent of departure from standard educational practice that the proposed research involves and the need for the exception.

Greater than Minimal Risk Research

For research that qualifies as greater than minimal risk, an investigator may not enroll as a research participant (1) any JHU student whom the investigator supervises academically or (2) any undergraduate student. There are two exceptions to this policy, one concerning research that may provide a direct medical benefit to participants and the other having to do with educational research.

Restriction on the enrollment of JHU students in greater than minimal risk research is not intended to bar students from participating in research that may provide a direct medical benefit. When it is in the medical best interests of JHU students to enroll in greater than minimal risk research, HIRB may permit their enrollment. When applicable, investigators should make the case in their application for HIRB approval that possible direct medical benefits justify the participation of JHU students.

For educational research that is greater than minimal risk, HIRB may grant an exception to the prohibition against the recruitment of students by academic supervisors if the research question is directed to a concern or problem that is specific to students as a group and the concern under investigation can only be addressed by research involving the students. For example, if the concern is stress and mental health problems among medical students, HIRB may allow JHU medical students to enroll in research that is aimed at evaluating an educational intervention intended to

decrease stress in medical students even if the research will collect sensitive information about mental health and drug use that might pose more than minimal risk to participants.

Confidentiality

Whenever JHU students participate in research, regardless of the risk level or prospect of direct medical benefit, investigators must provide the HIRB with specific plans for ensuring that the privacy of the students will be respected. These plans must take into account and adequately address the special concerns raised by the educational context.

HIRB Approval

The HIRB review and approval process for studies involving JHU students as participants does not differ from that for other studies unless the study constitutes educational research. The JHU policy concerning the recruitment and enrollment of students states that the Dean(s) of the JHU divisions in which the investigators have an appointment and Dean(s) of the division(s) with which the students are associated should be notified.

Research projects that HIRB determines to be exempt from Federal regulations governing human participant research are likewise exempt from JHU policies governing the recruitment and enrollment of JHU students, although the HIRB may require specific additional protections to be implemented

10.4 Recruitment and Enrollment of JHU Employees

Ethical concerns also arise when JHU employees are recruited as participants for Homewood research studies. These concerns relate primarily to possible undue pressure to enroll and invasion of privacy. The *Johns Hopkins University Policy Governing the Recruitment and Enrollment of Employees in Research Involving Human Subjects* is designed to protect employees from these risks. The policy defines an employee as, “an individual who is contracted to receive a salary or other compensation from Johns Hopkins University, Johns Hopkins Hospital, Johns Hopkins Health System, or any subsidiary thereof in return for services performed on a full-time, part-time, limited-time, temporary, contracted, or casual basis.” The policy defines direct supervision as, “having the authority to evaluate performance, recommend pay raises and/or promotions, or hire and fire employees.”

Note: This policy also applies to immediate family members of JHU employees.

Recruitment

JHU employees may not be directly solicited in research, regardless of the level of risk. Acceptable recruitment methods include the posting of IRB-approved flyers and the placement of IRB-approved advertisements.

Minimal Risk Research

Enrollment in research that an IRB has determined to be minimal risk is open to all JHU employees.

Greater than Minimal Risk Research

JHU employees may not enroll in research that an IRB has classified as greater than minimal risk if an investigator (principal or co-investigator) of the research directly supervises them as employees.

JHU employees also may not enroll in research that is greater than minimal risk if their direct supervisor reports to an investigator (principal or co-investigator) of the research. For example:

- Division X consists of a Division Head (Dr. A), faculty members (Drs. B, C, and D), and several fellows. Drs. A, B, C, and D all have administrative and research staff.
 - a. No employee of Division X may enroll in greater than minimal risk research in which Dr. A is a primary or co-investigator. However, Dr. A and his/her staff may enroll in greater than minimal risk research in which Dr. B, C, or D is a primary or co-investigator.
 - b. Dr. B may enroll in greater than minimal risk research in which Dr. C or D is a primary or co-investigator. Similarly, Dr. B's staff may enroll in greater than minimal risk research in which Dr. C or D is a primary or co-investigator. However, if Dr. B is a co-investigator in Dr. C's research, then Dr. B's staff may not enroll in Dr. C's research if that research is greater than minimal risk.
 - c. Fellows of Division X may not enroll in greater than minimal risk research in which Drs. A, B, C, or D are primary or co-investigators.

There are two exceptions to the above policy.

1. ***Research that offers a reasonable prospect of direct medical benefit to research participants.*** Restrictions on the enrollment of employees in greater than minimal risk research is not intended to bar an employee from participating as a research participant where it is in the medical best interests of the employee to do so. Investigators need to notify and seek the approval of the IRB in such exceptional circumstances.
 - ***IRB Waiver.*** An IRB has the authority to waive restrictions on the enrollment of employees in greater than minimal risk research ***under exceptional situations only*** where the IRB determines that the research is of significant importance and cannot be conducted without the enrollment of these employees.

Confidentiality

Whenever employees participate in research, regardless of the level or risk or prospect of direct medical benefit, investigators must provide the IRB with specific plans for ensuring that the privacy of these employees will be respected. These plans must take into account and adequately address the special concerns raised by the workplace context.

10.5 Payment to Participants

Federal regulations neither endorse nor prohibit compensation of research participants. DHHS regulations only require that consent be obtained under conditions that minimize coercion and undue influence. FDA regulations require that IRBs review the amount, method, and timing of payment to ensure that these are not coercive and do not create undue influence.

Any payment or incentive, whether financial or nonmonetary, that is offered for participation should be described in detail in the research protocol and explained in the consent documents. Details about payments should include the total to be paid for completion of the study, any prorating of payments, and the payment schedule. HIRB considers each proposal for payment of research

participants on a case-by-case basis and reserves the right to require that a monitor observe or supervise participant recruitment to ensure that payment is not overly influential.

The following guidelines are not meant to endorse or condone payment of participants but rather to establish guidelines for payments should investigators propose them.

- Payment must not be coercive or be used as an undue inducement to participate in research.
- The amount of payment may be stated on recruitment flyers but should not be emphasized. (See Recruitment Materials in Section 10.1.)
- The amount paid is not considered a benefit. It should fairly reflect the time that will be invested by the participants, the burden that will be imposed upon them by the research procedures, and other inconveniences they may experience as study participants, especially when the study offers little or no prospect of a direct health benefit to them.
- Payment may be in cash or in kind, such as food or clothing. Small gifts, such as movie passes, toys, and gift certificates, also may be appropriate.
- Payments should be sensitive to the local culture and participants' living conditions.
- Vulnerability of the study population should be taken into account, including medical, employment, and educational status and financial, emotional, and community resources.
- Participants who leave a study early, for any reason, should be paid on a reasonable prorated basis to avoid the impression that the investigator is coercing them to continue in the study or is punishing them for dropping out.
- Payment to persons who fulfill all study requirements may include a small additional amount for completion, provided it is not coercive.
- All information concerning payments, including the amount and disbursement schedule, should be described in the research protocol and consent documents.

10.6 Compensation for Injury

Whenever a project involves a procedure that may result in an injury to participants, the prospective participants should be advised as to the availability or unavailability of compensation for injury. Injury is not limited to physical harm. Investigators should also consider psychological, social, legal, and financial harm. Compensation may be in the form of payment and/or medical care. Participants should be made aware of (1) any medical treatments that are available should injury occur and (2) what the treatments consist of or where further information about them can be obtained. If the study is commercially funded, a description of the coverage that is available, if any, from the sponsor to the participant in case of injury and how to obtain further information about this coverage should be specified. The study sponsor typically will provide the specific language to describe the compensation it offers.

If no compensation is available, which typically is the case for studies reviewed by HIRB, participants must be informed that there is no commitment to provide free medical care or payment for any unfavorable outcomes resulting from participation in the research. Medical services will be offered at the usual rate.

10.7 Right of Participants to Withdraw

Consent is an ongoing process. Participants have the right to withdraw from a study at any time and should be informed of this right during the consent process. However, participants may forget this right during the course of a study. Investigators should consider whether and how to remind participants of the right to withdraw. If the research involves greater than minimal risk, participants' consent may need to be renegotiated at a specific point during the study or if triggered by certain events, such as an unanticipated problem or the emergence of new information relevant to the study. Investigators should consider if and when re-consent should occur. Re-consent may be required by HIRB and is subject to HIRB approval.

Federal regulations require that investigators give participants any new information that emerges from the study in which they are enrolled or from other research that may affect their decision to continue participating in the study. For instance, if an unexpected side effect to a treatment is observed, participants likely need to be informed of this side effect and may need to be re-consented. Investigators should report the unexpected side effect by filing an unanticipated problem report with HIRB in which they recommend whether participants should be notified. HIRB will make the final determination and must approve what will be communicated to participants.

Decisionally-impaired, seriously ill, and other vulnerable participants, such as children, may not be capable of evaluating whether they should continue participation in a study. Their legally authorized representative (LAR) or another person approved by HIRB may need to monitor their participation, periodically evaluate whether they should continue, and request withdrawal if needed.

Applicable Regulations & Guidelines

45 CFR 46.116

Johns Hopkins University Policy Governing the Recruitment and Enrollment of Employees in Research Involving Human Subjects [<http://jhuresearch.jhu.edu/policies.htm#jhuinternal>]

Johns Hopkins University Policy Concerning the Recruitment and Enrollment of Students in Research Involving Human Subjects [<http://jhuresearch.jhu.edu/policies.htm#jhuinternal>]

Resources & References

NIH (October, 2001). *NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research*.

[http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm]

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Section Eleven: Vulnerable Populations
Date of Revision: 11/16/14

Introduction

Federal regulations include specific provisions for the protection of special populations that are potentially more vulnerable than others to coercion, undue influence, and harm from research. The vulnerable populations specifically protected in Federal regulations are children [45 CFR 46, Subpart D]; pregnant women, fetuses, and neonates [45 CFR 46, Subpart B]; prisoners [45 CFR 46, Subpart C]; as well as mentally disabled persons and economically or educationally disadvantaged persons [45 CFR 46.111].

Section Objective

In this section, the additional safeguards that must be considered in research with vulnerable populations are described. Each of the following populations is addressed: children; pregnant women, fetuses, and neonates; prisoners; and decisionally-impaired individuals. In addition, special considerations for other potentially vulnerable populations, such as economically and educationally disadvantaged individuals, are discussed.

Relevant Definitions

ASSENT Affirmative agreement by an individual, such as a child or cognitively-impaired person, who is not competent to give legally valid informed consent to participate in research. Failure to object to participation absent affirmative agreement does not qualify as assent.

CHILDREN Individuals who have not attained the legal age for consent to treatment or procedures involved in research according to applicable law of the jurisdiction in which the research will be conducted. In Maryland, individuals 18 years of age and older are of legal age (released from parental authority) and considered adults [http://mlis.state.md.us/cgi-win/web_statutes.exe - section 24]. (Also called **MINORS**.) There are several exceptions, such as marriage and childbearing, that can qualify individuals under the age of 18 as emancipated minors.

GUARDIAN An individual who has the legal authority according to state or local laws to consent on a child's behalf to general medical care and, by extension, to consent to the child's participation in research [45 CFR 46.402].

LEGALLY AUTHORIZED REPRESENTATIVE (LAR) An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to the participant's participation in a research study [45 CFR 46.102].

MINIMAL RISK When the probability and magnitude of anticipated physical or psychological harm or discomfort in the proposed research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests [45 CFR

46.102]. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of a routine physical examination.

MINIMAL RISK AS IT APPLIES TO PRISONER PARTICIPANTS The probability and magnitude of physical or psychological harm is equivalent to that normally encountered in routine daily life of nonincarcerated individuals or in the routine medical, dental, or psychological examination of healthy, nonincarcerated persons. The risks to which prisoners are routinely exposed in their daily lives are not the standard used to define minimal risk for prisoners [45 CFR 46.303(d)].

PARENT The biological or adoptive mother or father of a child.

PERMISSION Consent of parent(s) or guardian to the participation of a child or ward in research [45 CFR 46.402(c)].

PRISONERS Individuals involuntarily confined in a penal institution, including individuals sentenced under a criminal or civil statute or detained pending arraignment, trial, or sentencing [45 CFR 46.303(c)]. The term also applies to individuals detained in other facilities, such as drug detoxification or alcoholism treatment centers, under statutes or commitment procedures that provide these as alternatives to incarceration in a penal institution or criminal prosecution.

WARD OF THE STATE Individual in state custody, whose rights and safety are guarded by the state (e.g., minor, mentally incompetent person).

11.1 Children

The unique vulnerability of children requires that they receive additional protections when they are being considered as potential research participants. Federal regulations require that (1) to the extent that they are able, children be given the opportunity to agree or disagree to take part in the research and (2) the permission of their parents or guardians be obtained, except under specific circumstances in which the IRB is permitted to waive the parental permission requirement. Furthermore, risks associated with the research must be compared with those encountered in the daily lives of children and must be justified in relation to the anticipated benefits of the study.

While HIRB and investigators must pay careful attention to these additional requirements, children should not be denied the benefits of participating in research. Children should be included in human research activities unless there is an appropriate justification for excluding them, such as the need to first conduct the research in adults or because the research does not apply to children.

Justifications for Excluding Children from Research

The following is an exhaustive list of appropriate scientific or ethical justifications for excluding children from research:

1. The research topic is irrelevant to children (e.g., research on full-time employment or adult-onset diseases).
 - There are laws or regulations that bar the inclusion of children in the research.
 - The knowledge being sought in the research is already available for children or will be obtained from another ongoing study, and an additional study would be redundant.
 - A separate, age-specific study in children is warranted and preferable.

- Insufficient data are available in adults to judge potential risks in children. (One of the research objectives might be to obtain sufficient adult data to make this judgment.)
- The study is designed to collect additional data on pre-enrolled adult study participants.

There are other special cases that can be justified by the investigator.

Allowable Categories of Research Involving Children

Investigators planning to conduct research with children must submit a completed Child Checklist with their HIRB application for new research. The checklist outlines the Federally allowed categories of research involving children and the conditions for obtaining child assent and permission of parents or guardians as follows:

1. Research involving no more than minimal risk [45 CFR 46.404]. This requires that:
 - Assent of the child and permission of at least one parent or guardian are obtained.
 - Research involving greater than minimal risk that presents the prospect of direct benefit to individual participants [45 CFR 46.405]. This requires that:
 - The risks are justified by the anticipated benefits.
 - The relation of risks to benefits is at least as favorable as any available alternatives.
 - Assent of the child and permission of at least one parent or guardian are obtained.
 - Research involving greater than minimal risk that has no prospect of direct benefit to individual participants but is likely to yield generalizable knowledge about the children's disorder or condition [45 CFR 46.406]. This requires that:
 - The risks represent only a minor increase over minimal risk.
 - The intervention or procedure consists of experiences that are reasonably commensurate with those inherent in participants' actual or expected medical, dental, psychological, social, or educational settings.
 - The intervention or procedure is likely to yield generalizable knowledge about the participants' disorder or condition that is of vital importance for the understanding or amelioration of the disorder or condition.
 - Assent of the child and permission of both parents or a guardian are obtained, 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.
 - If the research does not fit into one of three previous categories, HIRB must either disapprove the research or refer the study to the Secretary, DHHS, if it finds that the research presents a reasonable opportunity to understand, prevent, or alleviate a serious problem affecting the health and welfare of children [45 CFR 46.407]. The Secretary, DHHS, will grant approval only after review in consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following publication and public comment. For this category of research, the assent of the child and permission of both parents or a guardian must be obtained 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.

Child Assent/Parental Permission

Federal regulations require that (1) to the extent that they are able, children be given the opportunity to agree (i.e., assent) or disagree to take part in research and (2) the permission of their parent(s) or guardian be obtained unless waiver requirements have been satisfied. All of the requirements concerning informed consent apply to parental permission (i.e., the required elements of informed consent must be included in parental permission forms). Templates for parental permission and assent forms are available on the HIRB Web site. The waiver options for informed consent also apply to parental permission.

HIRB requires that assent be obtained from children ages 7 years or older. The form and content of the assent depends on the age of the child. Younger children cannot provide assent, but they should be appropriately informed of study procedures to the extent possible.

Children younger than 7 years. A simple oral explanation should be offered to the child before study-related procedures are conducted unless the child is too young to understand such an explanation. For instance, for a study of cognitive development, the child may be told: “We are going to show you a video while you sit in your mom’s [or other caregiver’s] lap. After the video, we will ask you some questions about what you saw.” The simple oral explanation should be included in the HIRB application.

Children 7 to 11 years. Informed voluntary verbal assent should be obtained from the child without pressure from parents or investigators. The HIRB application should include an example of the explanation to be offered to the child. A sample child assent form is available on the HIRB Web site. Assent from the child should be solicited and recorded in the presence of a parent, and the parental permission form should include a statement such as follows: “This study has been explained to my child in my presence, in language s/he can understand. S/he has been encouraged to ask questions both now and in the future about the research.”

Children 12 to 15 years. Investigators may choose to handle the consent/assent requirements for this group in one of two ways. They may submit either (1) a consent form that is written at a level simple enough for both the parent(s) and child to read and understand (e.g., about a 6th-grade reading level) or (2) a permission form for one or both parents to sign and a separate assent form for the child to sign. If a permission form is designed for both parent(s) and child, it should be signed by each after the study has been explained. The permission form should be written as simply as possible and should cover the following points:

- What the study is about.
- Why the child was selected for the study.
- That taking part in the study is voluntary.
- What procedures will be done.
- Potential benefits of the study.
- Potential risks of the study.

- Assurance that the child will be treated the same whether or not the child agrees to participate in the study.
- An invitation to ask questions about the study.
- Assurance that the child may withdraw from the study after discussing withdrawal with her or his parent(s).

Children 16 to 18 years. A permission form written in language that is easily understandable to both the parent(s) and child is sufficient for this group. A separate assent form need not be used. The parent(s) and the child must sign the consent form.

Child Consent Without Parental Permission

Under certain conditions, children may be able to consent to research without parental permission. Investigators should consult state and local laws and regulations for exceptions to obtaining parental permission. If a waiver of parental permission is requested, a concise but complete justification must be provided to HIRB. The following is a list for Maryland of the most common research situations in which a child may be able to consent to participate in research without parental permission:

- The child is not living with and is financially independent from parent(s) and/or guardian.
- The child is pregnant, and the research and treatments concern her pregnancy.
- The child wants specific treatment or advice about drug abuse, alcoholism, sexually-transmitted diseases, pregnancy, or contraception (other than sterilization).
- The child is at least 16 years old, and the research consists of consultation, diagnosis, and/or treatment of a mental or emotional disorder by a physician, psychologist, or a clinic.
- The child is validly married or is a parent.

There are additional limited situations in which children may consent to participate without parental permission. Please contact the HIRB Office for further information.

Research Conducted in Public Schools

Investigators collecting data in public schools and private schools that receive Federal money are responsible for ensuring that the schools comply with the Family Educational Rights and Privacy Act (FERPA) and the Protection of Pupil Rights Amendment (PPRA). FERPA controls access to and disclosure of personally identifiable student information and records; PPRA controls the development and administration of surveys that involve protected information in local educational agencies (i.e., school systems) and schools. The letter of cooperation from the public school or school system official should include a statement that the school complies with FERPA and PPRA, in addition to a statement that the school or school system supports the research.

Under FERPA, with certain exceptions, the permission of parents or guardians must be obtained before students' record or personally identifiable information is disclosed. Under PPRA, the permission of parents or guardians must be obtained, or in some cases the parents or guardians must

be allowed to exclude their children, if an investigator develops or administers a survey for students that covers one of the following areas of protected information:

1. Political affiliations or beliefs of the students or students' parents.
 - Mental or psychological problems of the students or students' family.
 - Sexual behavior or attitudes.
 - Illegal, anti-social, self-incriminating, or demeaning behavior.
 - Critical appraisals of other individuals with whom the students have close family relationships.
 - Legally recognized privileged or analogous relationships, such as those with lawyers, physicians, or ministers.
 - Religious practices, affiliations, or beliefs of the students or students' parents.
 - Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such a program).

Obtaining informed consent may be especially difficult when recruiting students from a school or school system. It is imperative that investigators obtain signed parental permission prior to obtaining assent from students. This may be accomplished by giving students letters containing permission forms to take home to their parents.

More information regarding FERPA can be found online [<http://www.ed.gov/policy/gen/guid/fpco/ferpa/index.html>]. More information on PPRA also can be found online [<http://www.ed.gov/policy/gen/guid/fpco/ppra/index.html>].

Wards of the State

Children who are wards of the state or any other agency may be included in the allowable categories of research involving children if the research is (1) related to their status as wards or (2) conducted in settings in which the majority of children who are participants are not wards. Investigators must make provisions for a child advocate for each child who is a ward. The advocate may not be the child's guardian or a person acting in loco parentis.

11.2 Pregnant Women, Fetuses, and Neonates

Pregnant women should be given the same opportunity as nonpregnant women to participate in and experience the benefits and burdens of research. Pregnant women are, however, a vulnerable population and Federal regulations require that additional protections be provided for them when they take part in research. State and local laws may also require additional considerations for research that involves pregnant women. HIRB reviews all nonbiomedical research involving pregnant women and women who may become pregnant and includes among its members individuals who work with pregnant women and/or neonates.

General Guidelines

- Pregnant women should be included in all research unless there are valid reasons for excluding them. Inclusion of women who are, or may become, pregnant is important so

that research findings can be generalizable and of benefit to all persons at risk of the condition under study.

- Generally, pregnant women may be included in research that poses no greater than minimal risk to the fetus.
- The specific guidelines in this section for pregnant women, fetuses, and neonates do not apply to research that is exempt from Federal regulations.

Research Involving Women Who Are, or May Become, Pregnant

Investigators who plan to involve pregnant women or women of childbearing potential in their research should consider the safety implications of pregnancy. There are several different categories of research that include pregnant women and/or women of childbearing potential.

Studies in which pregnancy is coincidental to participant selection. Any study that includes women of childbearing potential could, by chance, include women who are pregnant or become pregnant during the study. If the study poses greater than minimal risk, participants should be advised during the informed consent process and in consent forms that a particular treatment or procedure “may involve risks to the participant (or the embryo or fetus if the participant is or becomes pregnant) that are currently unforeseeable.”

Studies in which pregnancy is an exclusion criterion. For studies in which pregnant women are to be excluded because of unacceptable risk to the woman or fetus, nonpregnant participants of childbearing potential may need to be instructed on methods to avoid pregnancy while involved in and following the research. Investigators may need to require testing to determine that a woman is not pregnant prior to enrollment and during the study.

Studies directed primarily toward the health of pregnant women. Research may be undertaken to explore how women’s health is affected by pregnancy. In such research, a woman’s needs generally take precedence over those of the fetus. HIRB will, however, strive to ensure that risks to the fetus are minimized.

Studies directed toward pregnancy. Some studies examine the normal and abnormal processes of pregnancy, labor, and delivery. For these studies, HIRB must determine that the risk to the fetus does not exceed the risk from established procedures routinely used in uncomplicated pregnancies or in pregnancies with complications comparable to those being studied.

Pregnancy Testing

Pregnancy testing may be necessary in research that excludes pregnant women. The following methods for determining that a woman is not pregnant are no longer acceptable: (1) self-reporting by the participant and (2) reliance on the participant’s recent menstrual history. The only acceptable method to determine that a woman is not pregnant is to perform a urine pregnancy test on the day the study commences and to exclude potential participants who test positive. If a study involves a procedure or treatment that is contraindicated during pregnancy, the urine pregnancy test should be done each time the procedure or treatment is administered. Testing should occur on the same day as the treatment or procedure.

Allowable Research Involving Pregnant Women or Fetuses Prior to Delivery

HIRB may approve research involving pregnant women or fetuses prior to delivery if the following conditions are satisfied:

- All risks are the least possible for achieving the objectives of the research.
- Where scientifically appropriate, prior studies in animals and nonpregnant women provide a basis for assessing the risks to pregnant women and fetuses, and the risks are the least possible for achieving the objectives of the study.
- Risks to the fetus are no greater than minimal, and the risks are caused solely by interventions or procedures that hold out the prospect of direct benefit to the woman or fetus; OR if there is no prospect of direct benefit to the woman or fetus, the risks to the fetus are no greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.
- Investigators will have no part in decisions regarding ending the pregnancy or in determining the viability of a fetus.
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy.
- The consent document includes a clear explanation regarding the reasonably foreseeable impact of the research on the fetus and neonate.
- The informed consent of the pregnant woman or her legally authorized representative (LAR) must be obtained if *any* one of the following is true:
 - a. The research holds out the prospect of a direct benefit to the pregnant woman.
 - b. The research holds out the prospect of a direct benefit both to the pregnant woman and the fetus.
 - c. The research does not hold out the prospect of direct benefit to the woman or the fetus, but the 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.
- If the research holds out the prospect of a direct benefit solely to the fetus, the informed consent of the pregnant woman (or her LAR) and the father must be obtained, unless the father is not reasonably available, is incompetent or temporarily incapacitated, or the pregnancy resulted from rape or incest, in which cases the father's consent is not needed. In cases where the father is not reasonably available, a statement to this effect must be signed by the mother.
- If the pregnant individual is a minor, the assent of the minor and parental permission must be obtained. State and local laws for parental permission and assent by the minor may additionally apply. If the research concerns the pregnancy, the consent of the minor alone is sufficient in Maryland.

Allowable Research Involving Neonates

Neonates of Uncertain Viability. HIRB may approve research with neonates of uncertain viability if *all* of the following conditions are met:

- Where scientifically appropriate, preclinical and clinical studies have been conducted which provide data for assessing potential risks to the neonate.
- If the research holds the prospect of enhancing survival of the neonate to the point of viability, the level of risk is the least possible for reaching that objective.
- If the research does not hold the prospect of enhancing the neonate's survival, its purpose is the development of important biomedical knowledge that cannot be obtained by other means, and the research does not create added risk for the neonate.
- Investigators will have no part in decisions regarding ending a pregnancy or in determining the viability of a fetus.
- The informed consent of at least one parent is obtained.

Nonviable Neonates. HIRB may approve research involving nonviable neonates if *all* of the following conditions are met:

- There will be no added risk to the neonate resulting from the research.
- Vital functions of the neonate will not be artificially maintained.
- The research will not terminate the neonate's heartbeat or respiration.
- The research seeks important biomedical knowledge that cannot be obtained by other means.
- Investigators will have no part in decisions regarding ending a pregnancy or in determining the viability of a fetus.
- The informed consent of both parents will be obtained, unless the father is not reasonably available, is incompetent, or is temporarily incapacitated, or the pregnancy resulted from rape or incest, in which cases his consent is not needed. If the father is not reasonably available, the mother must sign a statement to this effect. The consent of a legally authorized representative (LAR) of either parent of a nonviable neonate will not suffice.

Viable Neonates. Research on viable neonates is considered to be research on children. (See Children in Section 11.1.)

Allowable Research with Human Fetal Tissue, Placenta, or Post Delivery Fetal Material

- Some state and local laws and certain cultures ban or limit research that involves, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus. Such research must be conducted in accordance with all applicable Federal, state, and local laws and regulations regarding these activities, as well as with sensitivity to relevant cultural beliefs and practices.

- Research that involves human fetal tissue obtained after delivery (e.g., placenta, tissue from an induced or spontaneous abortion or a still birth) is evaluated by HIRB as research on tissue specimens. (See Research with Human Biological Materials in Section 7.6.) If the tissue or specimen is linked directly or indirectly through identifiers to living individuals, those individuals must be considered human research participants.

Allowable Research Not Otherwise Approvable

Research not otherwise approvable is research that presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates that cannot be approved within the criteria set forth above. The Secretary, DHHS, will conduct or fund research that HIRB cannot approve under the criteria outlined above if *all* of the following conditions are met:

- HIRB 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.
- The Secretary, DHHS, after consulting with a panel of experts in pertinent disciplines (e.g., science, medicine, ethics, law) and allowing opportunity for public review and comments, including a public meeting announced in the Federal Register, has determined that the study satisfies *all* of the following criteria:
 - d. 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.
 - e. The research will be conducted in accordance with sound ethical principles.
 - f. Informed consent will be obtained as described in this section.

11.3 Prisoners

Prisoners may be under constraints because of their incarceration that could affect their ability to make a truly voluntary and uncoerced decision to participate in research. Therefore, Federal regulations require that IRBs apply additional safeguards for the protection of prisoners involved in research. These requirements apply whether the research involves individuals who are prisoners at the time of enrollment or participants who become prisoners subsequent to enrollment.

Except as noted below, all research involving prisoners must be reviewed and approved by an IRB as research involving prisoners. This rule applies regardless of the funding source or whether prisoners are the recruited participant population or participants become prisoners following enrollment. As part of its reciprocity agreement with the Johns Hopkins School of Public Health Institutional Review Board, all research involving prisoners that would otherwise be reviewed by HIRB will be forwarded to JHSPH IRB.

Allowable Categories of Research Involving Prisoners

The categories of permissible research involving prisoners are as follows:

1. The research is minimal risk, no more than an inconvenience to participants, and a study of the possible causes, effects, and processes of incarceration and criminal behavior [45 CFR 46.306(a)(2)(i)].
 - The research is minimal risk, no more than an inconvenience to participants, and a study of prisons as institutional structures or of prisoners as incarcerated individuals [45 CFR 46.306(a)(2)(ii)].
 - The research is a study of conditions that especially affect prisoners as a class (e.g., vaccine trials relating to hepatitis; research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) [45 CFR 46.306(a)(2)(iii)].
 - The research is a study of practices, both innovative and accepted, that have the intent and reasonable probability of improving the health and well-being of participants. However, if the study involves a control group that may not benefit, it requires the additional approval of the Secretary, DHHS [45 CFR 46.306(a)(2)(iv)].
 - The research is Federally funded, minimal risk, and no more than an inconvenience to participants; prisoners are not a particular focus of the research; and the sole purpose of the research is to describe the prevalence or incidence of a disease by identifying all cases or to study potential risk factors associated with a disease [Federal Register, Vol. 68, No. 119 36929-31 6/20/03].

Additional Requirements for Research that Involves Prisoners

Investigators intending to involve prisoners in their research will need to complete the Prisoner Checklist and submit it with their applications for JHSPH IRB approval. Contact with prisoners may not begin until an IRB has approved the study. The IRB must make all seven of the following additional findings before granting approval:

1. The research fits into one of the above categories of permissible research with prisoners.
 - Any possible advantages accruing to prisoners through their participation in the research are not of such a magnitude, in comparison to the general living conditions, medical care, quality of food, amenities, and opportunity for earnings in the prison, that prisoners' ability to weigh the risks of the research against the value of such advantages in the limited-choice prison environment is impaired.
 - The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers.
 - Procedures for the selection of participants within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the PI provides the IRB with justification in writing for another procedure, control participants (if any) must be selected randomly from the group of available prisoners who meet the characteristics needed for the research project.
 - Information will be presented to prisoners in language that is understandable to them.
 - Adequate assurance exists that parole boards will not take into account prisoners' participation in the research when making decisions regarding parole, and each prisoner

is clearly informed in advance that such participation will have no effect on his or her parole.

- Where HIRB finds there may be a need for follow-up examination or care of participants following the end of their participation, adequate provisions have been made for such examination or care, taking into account the varying lengths of prisoners' sentences, and for informing participants of this fact.

Research Involving Participants Who Become Prisoners After Enrollment

If a Homewood PI becomes aware of a participant who becomes a prisoner after enrollment, the PI should notify the HIRB Office immediately. All research interactions and interventions with and obtainment of identifiable private information about the now-incarcerated prisoner-participant must cease until the additional requirements described above for research on prisoners have been satisfied with respect to the relevant protocol. In special circumstances in which the PI asserts that it is in the best interests of the participant to remain in the research study while incarcerated, the HIRB Chair or a JHSPH IRB Chair may determine that the participant should continue to participate in the research while the additional requirements are being satisfied. The study will need to be transferred from HIRB to a JHSPH IRB for review.

In certain populations, such as drug-users, the likelihood that some participants may become incarcerated while participating in a research project is high. If this is anticipated, the investigator may request that a JHSPH IRB review the study as research involving prisoners. HIRB may also note this possibility at the time of initial review and decide to forward the application to a JHSPH IRB. In either case, a JHSPH IRB would then review the application based on the additional Federal requirements for approval of research involving prisoners.

Required Review by OHRP

All research involving prisoners that is funded by DHHS must be reviewed and approved by OHRP, in addition to JHSPH IRB review and approval. The process is as follows:

1. HIRB forwards the application to a JHSPH IRB for review.
2. After JHSPH IRB approves the research, it sends a certified letter with a copy of the proposal to the Secretary (OPRR) to document that the research was reviewed and approved under 45 CFR 46.305.
3. The Secretary (OPRR) must determine that the proposed research falls within one of the categories of permissible research specified in 45 CFR 46.306(a)(2).
 - JHSPH IRB notifies the investigator of its recommendation and, once received, that of OHRP.

Note: DHHS-funded research with prisoner(s) may not proceed until JHSPH IRB and OHRP grant approval, unless participants become incarcerated after enrollment and the IRB Chair determines it is in the best interest of the participant(s) to proceed.

11.4 Decisionally-Impaired Participants

Individuals whose decision-making capacity is restricted, wholly or in part, due to illness, mental disability, or other circumstances may be incapable of making informed judgments about whether to

enroll or continue participation in a study. The Common Rule requires that additional safeguards be in place to protect the rights and welfare of individuals who may be subject to undue coercion or undue influence, including mentally disabled persons. There are, however, no additional DHHS regulations that specifically concern protection of participants who are unable to make informed decisions due to cognitive impairment or another disability.

HIRB considers decisionally-impaired individuals to be vulnerable and in need of additional protections. It has developed the following policy based on NIH guidance entitled, *Research Involving Individuals with Questionable Capacity to Consent: Points to Consider*. The policy includes, but is not limited to, the following categories of studies:

- Psychiatric studies, where it is anticipated (but not presumed) that patients may be or become decisionally impaired.
- Clinical protocols involving medical conditions that often, but not always, render a person physically unconscious or decisionally impaired (e.g., stroke, unstable or serious cardiac conditions, shock, trauma, drug abuse, fever, infections, and other reversible conditions causing changes in mental status).
- All other research that may include participants who might experience fluctuating decisional capacity (due to dementia, emotional distress, illness, etc.).

Selecting Participants and Obtaining their Consent

It should not be assumed that incapacitated or decisionally-impaired participants are incapable of giving valid initial or ongoing consent. Investigators who will conduct studies in which the decision-making capacity of some or all participants may be impaired, either prior to enrollment or during the course of the study, should address the following points in their research plan.

1. The research generally should be conducted on participants who have the capacity to consent before being conducted on participants who are unable to give consent.
 - The research protocol should describe procedures for assessing a participant's capacity to consent and the circumstances in which consent will be sought from a Legally Authorized Representative (LAR) recognized by the state in which the research will be conducted. Investigators should consider a two-part consent process when appropriate: (1) an assessment of comprehension and recall and (2) a test of understanding. Capacity should be determined in relation to the research tasks. For research protocols that present greater than minimal risk, HIRB may require that an independent, qualified professional assess the potential participant's capacity to consent. The protocol should describe who will conduct the assessment, the nature of the assessment, and the criteria for determining that an LAR is needed. HIRB will permit investigators to use less formal procedures to assess a potential participant's capacity if there are good reasons for doing so.
 - When potential participants are capable of making informed decisions about participation, they may accept or decline participation without the involvement of any third parties. No person who has the capacity to consent may be enrolled in a study without his or her informed consent.

- A person who has been determined to lack capacity to consent to participate in a research study must be notified of that determination before permission may be sought from his or her LAR to enroll the individual in the study. Furthermore, if permission is given by an LAR to enroll a person in the study, the potential participant must be notified. Should the person object to participating, her or his objection must be respected.
- If a research participant has fluctuating or limited decision-making capacity or is likely to become incapacitated during the study, investigators should establish and maintain communication with involved caregivers, consistent with the participant's level of autonomy and the need for confidentiality.
- Any objection to enrollment or continued participation in a study by a potential or actual participant must be respected. An investigator, acting with a level of care and sensitivity that avoids the possibility or appearance of coercion, may approach people who previously declined to participate or decided not to continue in a study to ask whether they have changed their minds.
- Research protocols should include a thorough justification of the research design, including a description of the prospective benefits and procedures designed to minimize risks to participants. The evaluation of benefits should distinguish possible direct medical benefits to the participant from other types of benefits. Studies that elicit symptoms, withdraw participants rapidly from therapies, use placebos, or expose participants to greater than minimal risks must be thoroughly justified. Individuals who have been determined to lack capacity to consent should not be enrolled in research that is unlikely to result in direct benefit to them, unless the research presents no more than minimal risk.

11.5 Other Vulnerable Populations

Children, pregnant women, fetuses, neonates, prisoners, and decisionally-impaired individuals are not the only populations that may warrant special protections. Individuals may also be considered vulnerable if they belong to economically or educationally disadvantaged populations. Economically disadvantaged individuals, for instance, may be unduly influenced to enroll in research by an offer of monetary compensation, especially if it is a large sum that appears excessive in relation to the effort required. Educationally disadvantaged individuals may be unduly influenced by an investigator to agree to participate in a study because of their inability to comprehend the written informed consent document. Both economically and educationally disadvantaged individuals may feel unduly influenced to participate if recruited one-on-one by an educated, well-to-do person in authority such as their health care provider. They may feel coerced to participate because they mistakenly believe they will lose health care or other benefits should they decline.

Investigators should consider additional safeguards for potentially vulnerable populations that are not specifically covered by Federal regulations and justify these safeguards in their research protocols. For instance, educationally disadvantaged participants who are unable to understand the written consent form may need the short consent form summary in order to give informed consent. At the same time, investigators must respect the autonomy of potentially vulnerable individuals and not be overly paternalistic. Investigators should not simply assume that individuals for whom special protections are not Federally required will be unduly influenced or easily coerced. Investigators must

demonstrate to HIRB knowledge of the vulnerability or lack thereof of the population(s) from which they intend to draw participants and the appropriateness of any proposed special safeguards.

Applicable Regulations & Guidelines

21 CFR 50, Subpart D

28 CFR 512

38 CFR 56.111(a)(3)

45 CFR 46.111

45 CFR 46 Subparts B, C, & D

Family Educational Rights and Privacy Act (FERPA)

[<http://www.ed.gov/policy/gen/guid/fpco/ferpa/index.html>]

OHRP (May 26, 2005). *Children Involved as Subjects in Research: Guidance on the HHS 45 CFR 46.407 (“407”) Review Process*. (For research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.)

[http://www.hhs.gov/ohrp/children/guidance_407process.html]

OHRP (May 23, 2003). *OHRP Guidance on the Involvement of Prisoners in Research*.

[<http://www.hhs.gov/ohrp/humansubjects/guidance/prisoner.htm>]

Protection of Pupil Rights Amendment (PPRA)

[<http://www.ed.gov/policy/gen/guid/fpco/ppra/index.html>]

Resources & References

OHRP Special Protections for Children [<http://www.hhs.gov/ohrp/children/>]

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Section Twelve: Adverse Events & Unanticipated Problems
Date of Revision: 11/16/14

Introduction

Federal regulations require that IRBs (1) review unanticipated problems that involve risks to research participants or others and (2) have procedures for informing Federal department or agency heads of unanticipated problems, when appropriate. Unanticipated problems can occur at the research site or elsewhere in all types of studies, including observational research, behavioral interventions, and clinical trials. The Homewood Institutional Review Board (HIRB) defines an unanticipated problem as any undesirable and unintended event that is or may be related to the study *and* is harmful or potentially harmful to one or more research participants or other individuals associated with the research. Investigators are required to report unanticipated problems promptly to HIRB and are reminded of this requirement in HIRB approval letters and the Investigator's Manual. Following review of an unanticipated problem, HIRB may require corrective actions.

Adverse events may be expected or unexpected. When unexpected, they qualify as unanticipated problems if they are or could be due to the research. Adverse events that are reasonably expected to occur as a result of study procedures must be described in the consent form and research protocol.

For studies involving greater than minimal risk, the research protocol must include description of how expected and unexpected adverse events will be monitored, analyzed, and reported. Detecting adverse events and unanticipated problems and reporting them to HIRB, study sponsors, and regulatory authorities are essential procedures for the protection of research participants.

Section Objective

The purpose of this section is to detail the monitoring and reporting of adverse events and unanticipated problems, HIRB responses to unanticipated problems, and HIRB reporting to JHU officials and outside agencies. The role of Data Safety Monitors (DSMs), Data Safety Monitoring Boards (DSMBs), and Safety Monitoring Committees (SMCs) for studies involving greater than minimal risk are described.

Relevant Definitions

The term *unanticipated problem* is not consistently defined by Federal regulations, sponsors, or other government and nongovernment institutions. The term *adverse event* does not appear in Federal regulations 45 CFR 46; however, it is widely used to describe undesirable effects on participants that are associated with interventions, especially in FDA-regulated and industry-sponsored clinical trials. For studies that it reviews, HIRB uses the following definitions:

ADVERSE EVENT (AE) A harmful event affecting one or more participants that may be associated with research interventions or other research procedures, including the handling of private

information. Examples include emotional distress, exacerbation of an existing mental disorder, a breach of confidentiality, and a complication from use of a medical device.

DATA SAFETY MONITORING BOARD (DSMB)/SAFETY MONITORING COMMITTEE (SMC) A group of scientists, physicians, bioethicists, statisticians, and/or other experts that collects and analyzes data during the course of a research project involving greater than minimal risk. The group monitors data for adverse effects and other trends (such as an indication that one treatment is significantly better than another, particularly when one arm of a trial involves a placebo control) that would warrant modification or termination of the study or notification of participants about new information that might affect their willingness to continue in the study. The group also monitors the confidentiality of participants' data to ensure their privacy.

DATA SAFETY MONITOR (DSM) A scientist, physician, bioethicist, statistician, and/or other expert who collects and analyzes data during the course of a research project involving greater than minimal risk. The individual monitors data for adverse effects and other trends that would warrant modification or termination of the study or notification of participants about new information that might affect their willingness to continue in the study. The DSM also monitors the confidentiality of participants' data to ensure their privacy.

EXPECTED ADVERSE EVENT An adverse event that is anticipated, usually based on previous studies, and described in the consent form, the study protocol, and the investigator's brochure in clinical studies of an investigational product. Expected adverse events include adverse events that are recognized during the course of a study; determined, after review by an IRB, not to require the study to be stopped or the intervention to be modified; and classified for the remainder of the study as expected adverse events.

INVESTIGATOR'S BROCHURE A compilation of clinical and nonclinical information relevant to the clinical use of an investigational agent, such as an Investigational New Drug (IND) [21 CFR 312.23 (5)]. Describes the rationale and features of the investigational agent in sufficient detail to allow investigators, regulatory authorities, institutional review boards, and ethics committees to assess the risks and benefits to participants. The investigator's brochure is a required component of an FDA IND application.

SERIOUS ADVERSE EVENT (SAE) An adverse event that involves death, is life threatening, requires inpatient hospitalization or prolongs existing hospitalization, causes a persistent or significant disability or incapacity, causes a congenital anomaly or birth defect, or, in the judgment of the investigators or safety monitors, significantly increases risk to study participants.

UNEXPECTED ADVERSE EVENT (UAE) An adverse event whose nature, severity, and/or frequency is unanticipated and thus not described in the information provided in the consent form, the research protocol, or the investigator's brochure in clinical studies of an investigational product. When definitely or possibly due to the research, a UAE qualifies as an unanticipated problem.

UNANTICIPATED PROBLEM Any undesirable and unintended event, such as a breach of confidentiality, that is or may be related to the research *and* is harmful or potentially harmful to one or more research participants or other individuals associated with the research. To qualify as an unanticipated problem, actual harm does not have to occur; risk of harm is sufficient. Adverse events (AEs) and serious adverse events (SAEs) that are unanticipated qualify as unanticipated

problems when they are or may be due to the research; this includes anticipated AEs and SAEs that are worse than expected in magnitude and/or frequency.

12.1 Adverse Events

An adverse event is a harmful occurrence affecting one or more participants that may be associated with research interventions or other research procedures, including the handling of private information. Examples include emotional distress, exacerbation of an existing mental disorder, a breach of confidentiality, and a complication from use of a medical device.

Adverse events can be expected or unexpected. An expected adverse event is one that is anticipated, usually based on previous research, and described in the consent form, the study protocol, and the investigator's brochure in clinical studies of an investigational product. These include adverse events that are recognized during the course of a study; determined, after review by HIRB, not to require the study to be stopped or the intervention to be modified; and classified as expected adverse events for the remainder of the study. An unexpected adverse event is one that is not anticipated and whose nature, severity, and/or frequency of risk are not described in the information provided in the consent form, the research protocol, or the investigator's brochure in the case of a clinical study of an investigational product.

Adverse events can be the result of (1) the interventions and interactions used in the research; (2) the collection of identifiable private information for the study; (3) an underlying disease, disorder, or condition of the participant; and/or (4) other circumstances unrelated to the research or any underlying disease, disorder, or condition of the participant. Only unexpected adverse events from categories (1) and (2) can qualify as unanticipated problems. Unanticipated problems must be actually or potentially due, at least in part, to the research procedures. It is important for investigators to know which adverse events qualify as unanticipated problems because these must be reported to HIRB in a timely manner using the Unanticipated Problems form. (See Unanticipated Problems in Section 12.2.)

Monitoring Adverse Events in Studies with Greater than Minimal Risk

Studies that are greater than minimal risk must have a plan for detecting and reporting adverse events (AEs) and serious adverse events (SAEs). Depending on the level of risk and the study design, safety monitoring may be done by a designated investigator in the study, an independent Data Safety Monitor (DSM), a Data Safety Monitoring Board (DSMB), or a Safety Monitoring Committee (SMC):

- Safety monitoring by a designated investigator or DSM is appropriate for most behavioral intervention studies.
- At a minimum, phase I and II clinical trials that are greater than minimal risk require a DSM.
- A DSMB or SMC is required for phase III controlled clinical trials in which mortality or major morbidity are primary or secondary endpoints, or where these outcomes are likely even when the study addresses lesser outcomes, such as the relief of symptoms.
- A DSMB or SMC should be considered for:

- a. Trials in which a DSMB or SMC can help ensure scientific validity, for example by performing interim analyses that may lead to revision of the study's design.
- b. Behavioral intervention studies that involve vulnerable populations or in which serious adverse events related to the intervention or study procedures are possible.
- c. Phase I and II clinical trials that are multi-site studies, are blinded, employ moderate or high-risk interventions, or involve vulnerable populations.

Data Safety and Monitoring Plan

The research protocol for studies with greater than minimal risk must describe the following:

- The name, affiliation, and expertise of the person or group who will be responsible for data safety and monitoring.
- The safety endpoints (i.e., AEs and SAEs) to be monitored.
- The frequency with which the monitor(s) will review aggregate summaries of expected AEs and SAEs (this should be based on the level of risk associated with the study and the nature of expected AEs and SAEs).
- The plan for promptly providing reports to HIRB of all safety monitoring reviews of AEs and SAEs.
- The plan for reporting to HIRB, within 10 days of being identified, any expected AEs or SAEs that occur more frequently or are more severe than anticipated. These qualify as unanticipated problems.

When a DSMB or SMC will be utilized, the protocol should, if possible, be developed with input from the DSMB or SMC chair and should describe the following additional items:

- The membership of the DSMB or SMC, clearly specifying the name, affiliation, and expertise of voting and nonvoting members.
- The schedule of DSMB or SMC meetings, including a provision for emergency meetings.
- The timing of any proposed interim analyses.
- Rules for stopping the study because the intervention is proven effective, ineffective, or unsafe, or because the study does not have sufficient power to achieve a meaningful assessment of the intervention.
- The plan for promptly providing all DSMB or SMC reports to HIRB.

HIRB may decide, on a case-by-case basis, the type of safety monitoring and the frequency of review of adverse events required for a specific study.

Who May Serve as a DSM or Member of a DSMB or SMC

DSM. The Data Safety Monitor is usually proposed by the PI or study sponsor. She or he must have appropriate expertise to detect and assess AEs and determine their possible relation to study interventions and other procedures.

DSMB/SMC. The chair of the DSMB or SMC may be proposed by the PI or study sponsor. The chair should agree upon the members selected by or with input from the PI and/or the study sponsor. DSMBs and SMCs usually have at least three independent voting members, including the chair, with expertise in biostatistics and research ethics. Larger, more complex studies require a larger membership with a wider range of skills. Representatives of the study sponsor and the research team may also serve on the DSMB or SMC but only as nonvoting members.

Conflicts of interest. The DSM and DSMB/SMC voting members should have no other role in the study and should be selected to avoid real or perceived financial, professional, or personal conflicts of interest. Examples of individuals with conflicts include the following:

- Individuals employed by, or with a financial interest in, the company supporting the study or producing a product being evaluated.
- Individuals who serve as academic advisors to or are the supervisors or teachers of any of the investigators.
- Persons who are investigators on related studies.
- Individuals who are related by blood, marriage, or other significant relationship to an investigator on the protocol.
- Individuals whose professional advancement is determined to an appreciable extent by any of the investigators.

Reporting Adverse Events

The following should be reported to HIRB within 10 days of detection via submission of an Unanticipated Problems form as described in Section 12.2:

- Death of a participant, unless study participants are expected to have significant mortality from their underlying condition and any connection between study procedures and the participant's death has been ruled out. Where doubt exists, the death should be reported.
- Unexpected adverse events that are or may be related to participation in the research and thus qualify as unanticipated problems.
- Expected AEs and SAEs that are more severe or occur more frequently than expected and described in the consent form, study protocol, or the Investigator's Brochure.

All other expected and unexpected adverse events (i.e., those that do not qualify as unanticipated problems) should be summarized and reported to HIRB at the time of continuing review. (See the Application for Continuing Review.)

Note: Expected AEs and SAEs do not need to be reported to HIRB using the Unanticipated Problems form unless they occur with unexpected frequency or magnitude, as stated above. If a Federal agency or other sponsor requires that reports of all AEs and SAEs be submitted to HIRB, these should be provided in aggregate on the sponsor's forms. HIRB will acknowledge their receipt in writing but will not review them. Investigators are required to summarize all adverse events, expected and unexpected, in their progress reports for continuing review, and HIRB will examine them during the continuing review process.

If applicable, all expected and unexpected AEs and SAEs should be reported to the DSM, DSMB, or SMC according to the agreed upon reporting schedule and format.

12.2 Unanticipated Problems

An unanticipated problem is any undesirable and unintended event that (1) is actually or potentially related to the research and (2) has harmed, posed risk, or continues to pose risk to one or more research participants or others (e.g., a research team member, participants' significant others). To qualify as an unanticipated problem, actual harm does not have to occur; risk of harm is sufficient. Unanticipated problems should be reported regardless of whether they occur during the study, after the affected individual(s) have completed participation or are no longer enrolled in the study, or after completion of the research.

What Needs to Be Reported

Unanticipated problems must be reported promptly to HIRB. Events that qualify as unanticipated problems are those that occur on- or off-site and, in the opinion of the PI, Data Safety Monitor (DSM), Data Safety Monitoring Board (DSMB), or Safety Monitoring Committee (SMC), meet *all* of the following criteria:

- Are unexpected.
- Harmed, posed risk, or continue to pose risk to study participants or others.
- Are definitely or possibly related to the conduct of the study.

Examples include:

- An adverse event (AE) or serious adverse event (SAE) that is more severe than expected.
- An AE or SAE that occurs more frequently than expected.
- Any accidental or unintentional change in the HIRB-approved protocol that involves risk to participants or others.
- Any deviation from the HIRB-approved protocol taken without prior HIRB review to eliminate apparent immediate hazards to participants.
- Any complaint from a participant that indicates an unanticipated risk.
- A breach of confidentiality (e.g., loss of a computer containing identifiable private data) that places participants at risk of emotional or social harm.
- A threat by a participant to harm himself or others.
- The misdiagnosis of a participant that potentially harms the participant or prevents the participant from receiving a beneficial treatment.
- An accident at the study site that injures a participant or someone else.

Who Should Report Unanticipated Problems

The PI usually reports unanticipated problems. Reports may, however, come from any source, including HIRB members, other investigators, DSMs, DSMBs, SMCs, research participants or their family members, Johns Hopkins personnel, and others. When a problem is first recognized by or

reported to the PI, it is the PI's responsibility to inform the HIRB Office and, when appropriate, the study sponsor.

When and How to Report Unanticipated Problems

Unanticipated problems should be reported to HIRB within 10 days of being detected. Reports by the PI of unanticipated problems should be made using HIRB's Unanticipated Problems form or a sponsor's form, provided it includes all the information requested in the HIRB form. Reports should be submitted to the HIRB Office and, for Federally-supported research, to the funding agency. Other study sponsors also may require notification of unanticipated problems. For FDA-regulated research, reports of unanticipated problems must be submitted to the FDA.

To reiterate, all of the following should be reported within 10 days of being detected:

- Death of a participant, unless study participants are expected to have significant mortality from their underlying condition and any connection between study procedures and the participant's death has been ruled out. Where doubt exists, the death should be reported.
- Other unanticipated problems that harmed, posed risk, or continue to pose risk to study participants or others.
- Expected AEs and SAEs that are more severe than expected and described in the consent form, study protocol, or the Investigator's Brochure in studies of investigational agents.
- Expected AEs and SAEs that occur more frequently than expected and described in the consent form, study protocol, or the Investigator's Brochure.

Note: Events that are expected and clearly due to the natural progression of the participant's underlying disease or condition need only be summarized in the Application for Continuing Review; however, where doubt exists and the event is serious, it should be reported.

Reporting for Multi-Site Studies and Coordinating Centers

For multi-site studies in which the PI is a JHU faculty member and HIRB serves as the IRB, the reporting of unanticipated problems is the same as for single-site studies. If the problem occurs at a non-JHU site, it must be reported to the local IRB according to local IRB regulations, as well as to the HIRB Office.

For multi-site studies in which HIRB does not serve as the IRB, HIRB does not need to receive or review individual reports. When any of the Homewood Divisions serves as the coordinating center for a multi-site study but there is no participant contact and JHU staff do not collect data, unanticipated problems should be reported to the local IRBs for the individual sites at which they occur. HIRB does not need to receive or review the reports.

12.3 HIRB Responses to Reports of Unanticipated Problems

When the HIRB Office receives a report of an unanticipated problem, including an adverse event that is more severe or occurs more frequently than expected, the HIRB Chair or a designated board member will review the report together with all relevant study records. The Chair (or designee) will review reports of deaths within 72 hours and all other reports within 10 days. If additional

information is required, the Chair (or designee) will request it. The Chair (or designee) will determine whether the problem requires review by the full board. Problems that are determined not to affect the study's ratio of risks to expected benefits and can be resolved or are not continuing will generally be resolved by the Chair or designee in discussion with the PI. When full board review is required, members will receive a summary of the problem, relevant details, and the corrective action(s) recommended by the Chair or designee. The full board will vote on any corrective actions, the PI will be notified in writing of HIRB's decisions, and the board's discussion and decisions will be noted in the minutes of the meeting.

In response to reports of unanticipated problems, including unexpected deaths and other unexpected adverse events, HIRB actions will range from acknowledgment of the report to termination of the study. HIRB may take, but is not limited to, the following actions:

- Acknowledge the report and take no further actions.
- Request additional information from the PI and DSM, DSMB, or SMC.
- Request a meeting with the PI and other parties.
- Monitor the study for additional similar problems.
- Recommend a change in the research protocol or consent form(s).
- Require that the protocol and consent documents be revised to include a newly defined expected adverse event.
- Require that information about the problem be provided to past study participants.
- Require that current participants be informed about the problem. (This is mandatory when the information may affect their willingness to continue to take part in the research.)
- Require that current participants be re-consented.
- Monitor consent procedures.
- Modify the continuing review schedule.
- Refer the issue to other organizational entities (e.g., the Institutional Official (IO), the JHU Office of General Counsel).
- Suspend enrollment or study procedures, pending collection of additional information and/or modifications to the study protocol and consent documents.
- Terminate the study.

12.4 Reporting Unanticipated Problems to JHU Officials and Outside Agencies

Reports of HIRB decisions and actions in response to reports of unanticipated problems are drafted by the Chair and reviewed and approved by the Institutional Officer (IO). The Chair signs the report to the PI. All reports to other JHU officials, Federal agencies, sponsors, and collaborating IRBs are signed by the IO and sent by mail. The HIRB Office facilitates the reporting process.

Reports will include the following elements:

1. The nature of the unanticipated problem.
 - The findings of HIRB and others who took part in the investigation.
 - A summary of the elements of the problem that required corrective action.
 - The corrective actions taken by HIRB.
 - The rationale for HIRB's actions.
 - Plans for further investigation or follow-up actions, if any.

Copies of reports will be placed in the HIRB files and sent to:

1. The PI.
 - The HIRB Chair.
 - The dean or director of the PI's division (when appropriate).
 - The chair of the PI's department (when appropriate).
 - The highest academic official of any collaborating institution(s) (when appropriate).
 - The chair of any collaborating IRB(s) (when appropriate).
 - The DSM or chair of the DSMB or SMC (when appropriate).
 - OHRP, with a cover letter signed by the IO.
 - The FDA, if the study is FDA-regulated, with a cover letter signed by the IO.
 - The JHU Office of General Counsel, if the report raises issues of legal liability or there is a threat or perceived threat of a lawsuit, with a cover letter signed by the IO.
 - The Homewood Research Projects Administration Office, if the study is sponsored, with a cover letter signed by the IO.
 - The study sponsor (when appropriate), with a cover letter signed by the IO.

The above reports shall be distributed within 10 days following HIRB's decision on action(s) to resolve the unanticipated problem.

Applicable Regulations & Guidelines

OHRP (May 27, 2005). *Guidance on Reporting Incidents to OHRP*.
[http://www.hhs.gov/ohrp/policy/incidreport_ohrp.html].

Resources & References

DSMB — detailed discussion of the role, composition, and function of a DSMB
<http://www.fda.gov/cber/gdlns/clindatmon.htm>].

Ellenberg, S. S., Fleming, T. R., & DeMets, D. L. (2003). *Data monitoring committees in clinical trials: A practical perspective*. Hoboken, NJ: John Wiley & Sons.

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Section Thirteen: Noncompliance
Date of Revision: 11/16/14

Introduction

All members of the Homewood Divisions who conduct human participant research are expected to comply with the highest standards of ethical and professional conduct; Federal, state, and local laws and regulations; and HIRB policies and procedures. PIs have primary responsibility for ensuring that their studies meet these standards. Failure to do so may create avoidable risks for study participants and may warrant corrective actions by HIRB, including suspension or termination of the study and restrictions on the use of study data. HIRB has the authority to prohibit investigators from publishing any findings from studies it determines to be noncompliant.

Noncompliance is failure to comply with relevant Federal, state, or local laws or regulations or HIRB policies and procedures during the conduct of human participant research. Noncompliance may range from minor or sporadic and neither increasing risk nor reducing benefits for study participants to serious or continuing and increasing risk and reducing benefits for study participants and compromising the integrity of the Homewood Human Research Protection Program (HRPP). Initiating human participant research and substantially amending study procedures or consent forms without prior HIRB approval are examples of serious noncompliance.

Section Objective

The purpose of this section is to describe the reporting process for reports and allegations of noncompliance of research projects with Federal, state, or local regulations or HIRB policies and procedures. HIRB's response to reports and allegations of noncompliance, including investigation, actions taken, and reporting to the Institutional Official, OHRP, and others, is detailed. In addition, HIRB procedures for handling complaints are presented.

Relevant Definitions

CONTINUING NONCOMPLIANCE A pattern of noncompliance that, in the judgment of the HIRB Chair or convened board, suggests that, without intervention, instances of noncompliance likely will continue. Continuing noncompliance includes failure to respond to a request to resolve an episode of noncompliance.

HRPP (HUMAN RESEARCH PROTECTIONS PROGRAM) The array of protections that are in place throughout the Homewood Divisions to ensure the rights and safety of human participants in research associated with the divisions.

INTENTIONAL NONCOMPLIANCE Fraud or deception by a member or members of the research team. The intent is usually to mislead study participants, investigators, study sponsors, or others regarding study procedures or results.

NONCOMPLIANCE Failure to comply during the conduct of human participant research with relevant Federal, state, or local laws or regulations or HIRB policies and procedures. Noncompliance can range from minor and sporadic to serious and continuing and may be intentional.

OHRP (OFFICE FOR HUMAN RESEARCH PROTECTIONS) An administrative office within the Department of Health and Human Services (DHHS). OHRP implements Federal regulations for the protection of human participants [45 CFR 46] and provides guidance on ethical issues in biomedical and behavioral research.

SERIOUS NONCOMPLIANCE Failure to follow Federal, state, or local laws or regulations or HIRB policies and procedure in the conduct of research, thereby increasing risks to participants, decreasing potential benefits to participants, and/or compromising the integrity of HRPP, in the judgment of either the HIRB Chair or the convened board.

13.1 Reports and Allegations of Noncompliance

Noncompliance is failure to comply during the conduct of human participant research with relevant Federal, state, or local laws or regulations or HIRB policies and procedures. Noncompliance can range in severity from minor or sporadic and neither increasing risks nor reducing benefits for study participants to serious or continuing and increasing risks and reducing benefits for study participants and compromising the integrity of the Homewood Human Research Protection Program (HRPP). Initiating human participant research and substantially amending study procedures or consent forms without prior HIRB approval are examples of serious noncompliance.

Noncompliance can be either reported or alleged.

- A **report** of noncompliance is an account of noncompliance that does not require further evidence to confirm but may require additional information to resolve. Such noncompliance may be due to honest error or lack of oversight, or it may be intentional. Reports of noncompliance typically are made directly by investigators or found within documents, such as continuing review applications, requests for study changes, reports of unanticipated problems, study audits, published reports, and student theses.
- An **allegation** of noncompliance is an assertion that requires investigation and evidence to verify. Alleged noncompliance may be found to be due to honest error or lack of oversight, or it may be intentional. Allegations of noncompliance may come from a variety of sources. These include, but are not limited to, investigators, collaborating researchers, study staff, research participants or their families, and HIRB staff. Allegations may be made anonymously. The person making an allegation is the complainant, and the person about whom the allegation is made is the respondent.

All reports and allegations of noncompliance should be made directly or promptly forwarded to the HIRB Director, who will ensure that they are properly handled. All reports and allegations of noncompliance are kept confidential to the extent possible.

13.2 Minor Noncompliance

Noncompliance is considered minor when it does not increase risks to participants, decrease potential benefits to participants, or compromise the integrity of the Homewood Human Research

Protection Program (HRPP). A delay in the payment of participants (compensation is not a benefit), conducting exempt research before obtaining the IRB determination that the research is exempt, and the addition of a trained research team member without prior HIRB approval are examples of minor noncompliance.

HIRB Response to Reports of Minor Noncompliance

Reports of minor noncompliance may be resolved by the HIRB Office. The HIRB Director or staff will work directly with the PI, other research team members, and, if necessary, study participants to remedy the problem. The incident and corrective action will be documented in writing by HIRB staff or the PI and provided to the HIRB Director for review. If, in the judgment of the HIRB Director, the reported noncompliance is not serious or continuing and the actions taken are adequate to resolve the problem, no further action is required. If, however, the problem is serious, continues without resolution, or contributes to a pattern of recurrent noncompliance, it will be referred to the HIRB Chair for evaluation and action as described for reports of serious and continuing noncompliance below.

HIRB Response to Allegations of Minor Noncompliance

For allegations of minor noncompliance, the HIRB Director or staff will compile relevant information and present the issue to the HIRB Chair. The HIRB Chair and/or the HIRB Director (or a designee) will promptly contact the complainant (unless anonymous), respondent, PI (who may also be the respondent), and, if necessary, other research team members to obtain a greater understanding of the facts surrounding the allegation and, if substantiated, the actions needed to remedy the minor noncompliance. The outcome of all communications and discussions will be documented in writing. The documentation will be factual and objective and will include timelines for resolution of outstanding issues (e.g., meeting dates, response deadlines). The Chair or Director (or a designee) will communicate the outcome of these discussions to the complainant, the respondent, and the PI, and copies will be placed in the HIRB study file.

If these initial steps do not result in resolution of the allegation or if, in the opinion of the Chair and Director, the complaint alleges greater than minor noncompliance, the issue will be investigated and actions taken as described below for serious, continuing, and intentional noncompliance.

13.3 Serious, Continuing, and Intentional Noncompliance

Serious and continuing noncompliance require a different level of response than minor noncompliance. Intentional also necessitates a different level of response.

Serious noncompliance. Serious noncompliance is failure to follow relevant Federal, state, or local laws or regulations or HIRB policies and procedures which, in the judgment of either the HIRB Chair or the convened board, increases risks to participants, decreases potential benefits, or compromises the integrity of the Homewood Human Research Protection Program (HRPP). Examples of serious noncompliance include but are not limited to the following:

- Initiating contact with human participants without formal HIRB approval for research that does not qualify for exempt status.
- Substantively modifying research plans or procedures without HIRB approval, except to eliminate immediate hazards to participants.

- Failing to report problems that are serious, unanticipated, and related to the research.
- Using consent forms not approved by HIRB.
- Breaching confidentiality or otherwise violating participants' privacy.

Continuing noncompliance. Continuing noncompliance is a pattern of noncompliance that, in the judgment of the HIRB Chair or convened board, suggests that without intervention, instances of noncompliance likely will continue. Continuing noncompliance also includes failure to respond to a request to resolve an episode of noncompliance.

Intentional noncompliance. Intentional noncompliance entails fraud or deception by a member or members of the research team. The intent is usually to mislead study participants, other investigators, study sponsors, or other individuals regarding study procedures or results.

HIRB Response to Reports of Serious and Continuing Noncompliance

A team that includes at least the HIRB Chair (or designee) and the HIRB Director will promptly review reports of serious or continuing noncompliance. The team will plan and carry out an investigation of the noncompliance and summarize its findings. The Chair (or designee) will lead the investigation and is the person primarily responsible for overseeing all follow-up actions and communication with the investigators until the issue is resolved.

An investigation normally begins with fact-finding through confidential correspondence or direct discussion with the PI. Other relevant persons may also be interviewed. This may lead directly to a plan for corrective action that would eliminate avoidable risks to study participants and may allow the research to continue. If the investigation does not lead to such a plan, the Chair will consult with HIRB to develop a recommendation for corrective action in accordance with HIRB policies and procedures and actions taken previously in similar situations. In uncertain cases, the HIRB Director or HIRB Chair may consult with the JHU Office of General Counsel. The full board must approve the plan for corrective action prior to implementation, unless the Chair (or designee) determines that corrective action is necessary prior to full board approval in order to eliminate immediate hazards to participants, in which case HIRB will review the corrective action and plan at the next full committee meeting.

The range of corrective actions that HIRB may take includes but is not limited to the following:

- Monitor and/or audit the study.
- Monitor the consent process.
- Modify the research plan.
- Modify the consent document(s).
- Modify the continuing review schedule.
- Require additional training in the responsible conduct of human participant research.
- Notify current participants when such notification may influence participants' willingness to continue taking part in the research.
- Suspend or terminate HIRB approval for some research activities or the entire project.

- Require the PI to destroy all research data that was collected while the study was without IRB approval

If the instance of noncompliance involves research being conducted without prior approval by HIRB, the research will be terminated as described in Section 13.4.

HIRB Response to Allegations of Serious and Continuing Noncompliance

For allegations of serious or continuing noncompliance that is not intentional, the investigation and possible actions by HIRB are as described above for reports of serious or continuing noncompliance with the inclusion of discussion or correspondence with and reporting of findings and conclusions to the complainant (unless anonymous) and the respondent.

HIRB Response to Possible Intentional Noncompliance

If, during an investigation of reported or alleged noncompliance, evidence is uncovered of possible research fraud (e.g., scientific misconduct, intentional fabrication, falsification, or plagiarism), this possibility must be reported immediately to the PI's dean or division director to be handled in accordance with that division's policies regarding research/scientific misconduct. Once the dean or division director's preliminary inquiry or investigation is complete, the HIRB Chair will be informed as to the resolution.

If, during HIRB investigations of reported or alleged noncompliance, an investigator is found to have engaged in intentional noncompliance that is serious or continuing, the HIRB Chair can forward the matter to the investigator's dean or division director to be handled in accordance with that division's policies regarding professional misconduct. In this case, the HIRB Chair will serve as the complainant and will be involved in the process.

13.4 Suspension and Termination of Studies (Withdrawal of HIRB Approval)

HIRB has the authority to suspend and terminate research that is (1) not being conducted in accordance with Federal, state, or local laws or regulations or HIRB policies and procedures (i.e., misconduct) or (2) has been associated with unexpected risk or serious harm to participants. Investigators must immediately stop suspended or terminated research, unless HIRB has approved continuation in order to protect the welfare of enrolled participants. No additional participants may be enrolled. No official of any division of JHU can overturn suspension and termination decisions approved by the full board. Terminations are final, and only HIRB can lift suspensions by full board approval. Investigators are responsible for notifying their funding agencies when HIRB approval is suspended or withdrawn.

HIRB also has the authority to suspend or terminate human participant research conducted by investigators in the Homewood Divisions without HIRB approval, including studies continued after an approval period has expired. If an investigator fails to submit a continuing review application or HIRB does not review and approve a submitted continuing review application by the end of the study's approval period, the research must stop, unless HIRB finds that it is necessary for the safety and well-being of participants to continue receiving treatment or interventions. The IRB may require the PI to destroy all data that was collected while the study was without IRB approval. Expiration of HIRB approval does not need to be reported to OHRP as a suspension of HIRB approval according to DHHS regulations.

If, in the judgment of the HIRB Chair, a report or allegation of noncompliance warrants suspension or withdrawal of HIRB approval before completion of the investigation of noncompliance in order to ensure the protection of the rights and welfare of participants, the Chair may suspend or withdraw HIRB approval with subsequent review by the full board.

If HIRB terminates a study, all enrolled participants with whom there is ongoing contact must be notified of the termination. If termination is likely to adversely affect the rights or welfare of these participants, HIRB will require procedures for withdrawal that protect them to the greatest extent possible. If follow-up of participants for safety or other reasons is permitted or required by HIRB, the participants must be informed not only that the study is being terminated but also that unanticipated problems involving risks to participants or others must be reported to HIRB.

13.5 Reporting Noncompliance to JHU Officials, OHRP, and Others

Serious or continuing noncompliance that involves risks to participants or others will be reported to the Office for Human Research Protections (OHRP). The report will contain the following elements:

1. The nature of the event.
 - The findings of HIRB or others who took part in the investigation.
 - A summary of the problems that require corrective action.
 - The corrective actions taken by HIRB.
 - Plans for further investigation or follow-up actions, if any.

Copies of the report and cover letter will be placed in the HIRB files and sent to:

1. The PI.
 - The HIRB Chair.
 - The dean of the PI's department or division (when appropriate).
 - The chair of the PI's department or director of the PI's division (when appropriate).
 - The highest academic official of any collaborating institution(s) (when appropriate).
 - The chair of the local IRB where the research is being conducted (when appropriate).
 - The chair of the study DSMB or SMC (when appropriate).
 - The FDA, if the study is FDA-regulated, with a cover letter signed by the JHU IO.
 - The JHU Office of General Counsel, if the report raises issues of legal liability or there is a threat or perceived threat of a lawsuit.
 - The study sponsor (when appropriate).
 - The Homewood Research Projects Administration Office (when appropriate).

If the investigation and decision on corrective actions require more than 30 days after the noncompliance is first reported or alleged, the Chair should provide OHRP and any Federal funding agencies with a preliminary report that describes the situation, indicates an investigation is in

progress, and provides a time frame for a follow-up report. Reporting will be completed within 30 days after the investigation is concluded and corrective actions have been agreed upon by HIRB. If corrective actions continue beyond this period, a supplemental final report will be prepared and submitted to OHRP and Federal funding agencies within 30 days after the corrective actions have been completed and approved by HIRB.

13.6 Complaints Regarding Human Participant Research

Complaints may be made about any category of research and may include anyone directly or indirectly involved in the research. Complaints may come from any source, including HIRB members, investigators, research participants and their family members, JHU employees and students, the media, anonymous sources, and members of the public.

When complaints are made to investigators, they have two options for notifying HIRB, depending upon the nature of the complaint. Complaints made to investigators that do not involve risks to participants or others and are not related to the study's risk/benefit ratio (e.g., a participant complains that interviews inconveniently take place early in the morning) can be reported in progress reports in continuing review applications. The PI is required to retain documentation of the resolution to any complaints in the protocol file. Complaints made to investigators that involve potential risks to participants or others or potentially affect the study's risk/benefit ratio must be reported to HIRB as soon as possible, but no later than 10 working days after the investigator first receives the complaint. Complaints can be submitted directly to the HIRB Office at 410-516-6580 or hirb@jhu.edu. Complaints made to JHU staff, administrators, and others should be brought to the attention of the HIRB Director without unnecessary delay.

HIRB will investigate all complaints received, directly and indirectly, regarding human participant research under its jurisdiction. The level of investigation will depend on the seriousness of the situation and the potential risks to participants. HIRB also will review complaints reported by researchers in progress reports submitted for continuing review and will evaluate whether the researchers underestimated the risk involved and/or did not satisfactorily resolve the complaints. Substantiated complaints that involve potential risks to participants or others or potentially affect the study's risk/benefit ratio will be further investigated through a direct audit conducted by HIRB, and actions will be taken as deemed appropriate by HIRB. For instance, if noncompliance is substantiated, the noncompliance procedures outlined earlier in this section will be followed. Researchers must cooperate with HIRB investigations by making themselves available to answer questions, making documents and data accessible, and responding to written requests for information in a timely manner.

All complaints will be handled in a confidential manner to the extent possible. This includes protecting the identity of whistle-blowers (i.e., individuals who notify HIRB of possible noncompliance with Federal, state, or local laws or regulations or HIRB policies and procedures).

Applicable Regulations & Guidelines

21 CFR 50

21 CFR 56 — especially 56.108 and 56.113

42 CFR 50 Subpart A

45 CFR 46 — especially 46.113

OHRP (July 10, 2002). *Compliance Activities: Common Findings and Guidance*.
[<http://www.hhs.gov/ohrp/compliance/findings.pdf>]

OHRP (July 11, 2002). *Guidance on Continuing Review*.
[<http://www.hhs.gov/ohrp/humansubjects/guidance/contrev2002.htm#WHAT%20CONSTITUTES%20SUBSTANTIVE%20AND%20MEANINGFUL>]

Resources & References

Amdur, R., & Bankert, E. (2002). *Institutional Review Board: Management and Function*. Boston: Jones and Bartlett Publishers.

Homewood Institutional Review Board

Standard Operating Policies & Procedures

Section Fourteen: Records & Documentation
Date of Revision: 11/16/14

Introduction

In order to ensure compliance with Federal regulations and protect the safety and confidentiality of human research participants, application-related records must be thoroughly maintained; HIRB determinations, motions, and actions need to be accurately documented; and HIRB policies and procedures must be carefully developed and approved.

Section Objective

The purpose of this section is to describe the records and documentation that are essential to HIRB's operation. As detailed below, HIRB Office staff members are responsible for maintaining office records; planning and implementing HIRB meeting agendas; preparing, securing approval of, and distributing HIRB meeting minutes; and overseeing the development and approval of HIRB policies and procedures.

Relevant Definitions

INSTITUTIONAL OFFICIAL (IO) For the JHU Homewood Schools, the IO is the Vice Dean for Research and Science Infrastructure in the Krieger School of Arts and Sciences. The IO has ultimate responsibility for the institutional commitment made in HIRB's Federalwide Assurance (FWA). The IO is authorized to assure HIRB complies with the terms of the FWA and is ultimately responsible for the review and oversight of human participant research conducted in association with or supported by the Homewood Divisions. The IO cannot be an IRB member or chairperson.

MINUTES Official record of the proceedings of a meeting.

OHRP (OFFICE FOR HUMAN RESEARCH PROTECTIONS) An administrative office within the Department of Health and Human Services (DHHS). OHRP implements Federal regulations for the protection of human research participants [45 CFR 46] and provides guidance on ethical issues in biomedical and behavioral research.

14.1 HIRB Office Records

The HIRB Office must maintain files in a manner that preserves a complete history of all HIRB actions related to the review of research protocols, including applications for continuing review, requests for amendments and changes, and unanticipated problem reports. The office must retain all applications and reports (regardless of whether they are approved) for at least three years. The office must retain all records of approved and conducted research projects for at least three years beyond completion of the research.

The HIRB Office must maintain the following items:

- Applications for new studies that HIRB has reviewed, including scientific evaluations, if any. For approved studies, all approved protocols and consent documents must be filed.
- Applications for amendments and changes and all HIRB-approved revised documents (e.g., advertisements, research protocol, consent forms).
- Applications for continuing review, which include progress reports.
- DSM, DSMB, and SMC reports.
- Reports of unanticipated problems, which include reports of injuries to participants.
- Summaries of significant findings that emerged during the course of research projects that could have affected participants' willingness to continue participation and, thus, were provided to them.
- Reports and allegations of noncompliance.
- Copies of all correspondence between HIRB and investigators and between HIRB and other key study personnel.
- Minutes of all HIRB board meetings in sufficient detail to show attendance at the meetings; HIRB actions; the vote on HIRB actions, including the number of members voting for, voting against, and abstaining; the basis for requiring revisions to or disapproving research projects; and summaries of discussions of controverted issues and their resolution.
- A list of HIRB members, including their names; earned degrees; representative capacities; curriculum vitae (CVs) or biosketches, including associations with JHU and current place of employment and position; relevant certifications and licenses; conflict of interest disclosures; confidentiality agreements (e.g., privacy statements); and documentation of IRB training. Changes in board membership must be reported promptly to OHRP.
- HIRB standard operating policies and procedures.

The HIRB Office must make all records accessible in a timely and reasonable fashion for inspection and copying by authorized representatives of any regulatory oversight agency.

14.2 HIRB Meeting Agendas

Following receipt and confirmation of completeness, the HIRB Office will place the items below on the next available full committee meeting agenda:

1. ***New applications.*** All new applications for human participant research that require full board review are entered on the agenda.
 - ***Continuing review applications.*** Continuing review applications for human participant research that were initially approved by the full committee are entered on the agenda. (Continuing reviews generally occur at the same level of review as the initial application. For example, a study that qualified initially for expedited review will continue to be reviewed at the expedited level unless significant changes have occurred that require full board review.)

- ***Major amendments and changes.*** All major amendments and changes to currently approved human participant research that affect the risks and benefits of the study or substantially change the specific aims or design of the research are added to the agenda.
- ***Unanticipated problems.*** All unanticipated problems involving risks to participants or others and expected AEs or SAEs that occur more frequently or are more severe than expected are placed on the agenda.
- ***Exempt and expedited review determinations.*** For the purpose of notification, exemption of research projects by the HIRB Director and approval of research projects by the HIRB Chair or a designated board member through expedited review are placed on the agenda. HIRB members and the IO are thereby notified of research proposals on which determinations have been made under exempt and expedited review.
- ***Notification of other approvals by the chair or designated reviewers.*** For the purpose of notification, decisions made by the Chair or a designated board member on minor amendments and changes, continuing review of expedited research, unanticipated problems meeting the criteria for expedited review, and study closures are placed on the agenda.
- ***Noncompliance.*** Any serious or continuing noncompliance with Federal regulations or HIRB policies and procedures is placed on the agenda.
- ***Audits and monitoring.*** The results of any auditing or monitoring activities are entered in the agenda. However, if information gained during the auditing or monitoring process indicates that research participants are potentially being exposed to unexpected serious harm, the Chair or a designated board member may suspend the project prior to the next regularly scheduled HIRB meeting, where the matter will be reviewed.
- ***Education.*** As necessary, the HIRB Director will schedule education for HIRB members on the agenda. Education may focus on changes in Federal regulations, application of HIRB policies and procedures, or other IRB-related matters.

It is the responsibility of the HIRB Office to create the agenda for HIRB meetings and ensure that all items in each of the aforementioned areas that are ready for full committee review are scheduled on the agenda and apportioned adequate time given their scope and complexity. The HIRB Office will assemble packets of review materials for distribution to the Chair and board members. The agenda and review materials will be distributed in a timely fashion, typically one week prior to the meeting, allowing members ample time for adequate review. An addendum will be added when necessary, and relevant materials distributed as quickly as possible. The time allotted items on the agenda will vary according to the scope and complexity of the matter under review. HIRB members should notify the HIRB Director if additional time for any agenda item is needed.

14.3 HIRB Minutes

HIRB Office staff attending the convened HIRB full committee meeting draft detailed minutes to document HIRB determinations and discussions. According to Maryland law, meeting minutes are publicly available. Therefore, names of HIRB members, PIs, and others are not recorded in the minutes. The minutes of all full committee meetings should contain the information specified below.

General Requirements

1. Attendance throughout the meeting, including (a) the initial and continued presence of a quorum, including at least one nonscientist; (b) whenever an alternate member votes; (c) when a member leaves the room; and (d) when a member absents him/herself during a vote due to a conflict of interest.
 - HIRB member conflicts of interest that are identified at the beginning of the meeting.
 - For each new or continuing research protocol discussed, the following when applicable:
 - The recusal of a HIRB member from the meeting due to a conflict of interest during the discussion and vote on the study.
 - Determinations, motions, and actions taken by HIRB.
 - The vote on these determinations, motions, and actions including the number of members voting for, voting against, and abstaining. (In order to document the continued existence of a quorum, votes should be recorded in the minutes using the following format: Total Votes = 15, For: 14, Against: 0, and Abstained: 1.)
 - Summary of discussion of any controverted issues and the resolution of these issues.
 - In discussions of suspensions and terminations (i.e., withdrawal of HIRB approval), summary of issues regarding procedures (e.g., treatment) that may need to be continued for some or all participants for safety reasons.
 - When a new or continuing research application is approved, satisfaction of the criteria for approval stipulated in regulations 45 CFR 46.111 (and 21 CFR 56.111 if applicable). (The minutes should document the criteria that have been discussed and met.)
 - When a new or continuing research protocol is approved, the level of risk (e.g., minimal or greater than minimal) and the appropriateness of the approval period to the level of risk.
 - When application revisions are requested or an application is disapproved, the basis for the revisions or disapproval and summary of discussion and resolution of controverted issues.
 - A list of research projects that have been determined to be exempt from 45 CFR 46 and studies that have been approved through expedited review since the previous board meeting.

Specific Findings

When HIRB is required to make specific findings, these findings should be fully documented in the meeting minutes and should include protocol-specific information justifying each of them as described below.

1. ***Waiver or alteration of informed consent requirements.*** When approving a procedure that waives or alters the requirements of informed consent, the minutes must document that HIRB made specific findings required in accordance with HIRB policies and procedures.

- ***Waiver of documentation of informed consent.*** When approving a procedure that waives the requirements for obtaining a signed consent document, the minutes must document that HIRB made specific findings required in accordance with HIRB policy.
- ***Research involving children.*** When approving research that includes children as participants, the minutes must document that HIRB made specific findings in accordance with HIRB policies and procedures.
- ***Wards of the state or other agency.*** When reviewing research involving children who are wards of the state or any other agency, institution, or entity, HIRB must find and document in the minutes that such research is related to the children's status as wards or conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards.
- ***Research involving pregnant women, fetuses, neonates, or research on transplantation of fetal tissue.*** When approving research involving pregnant women, fetuses, neonates, or the transplantation of fetal tissue, the minutes must document that HIRB made specific findings in accordance with HIRB policies and procedures.
- ***Research involving decisionally-impaired participants.*** When reviewing research involving individuals who are decisionally impaired, HIRB must find and document in the minutes that the capacity to provide informed consent will be determined and monitored throughout the study and LARs relied upon when appropriate.

Participation via Phone

At a full committee meeting in which HIRB members participate via telephone, meeting minutes must document that each HIRB member participating by phone:

1. Has received all pertinent material prior to the meeting.
 - Can actively and equally participate in the discussion of all protocols, in accordance with HIRB policies and procedures.

Distribution and Approval of Minutes

The following steps are taken to distribute and approve HIRB meeting minutes:

1. HIRB Office staff complete a draft of the HIRB meeting minutes and forward the draft to all HIRB members who were present at the convened meeting.
 - HIRB members review the minutes and communicate any necessary revisions to HIRB Office staff.
 - HIRB Office staff e-mail the final version of the minutes to HIRB members prior to the next convened meeting.
 - HIRB members vote for approval of the final version of the minutes at the following convened meeting. (Only those members who were present at the meeting documented in the minutes may cast a vote. Members who were not present must abstain from the vote.)

- Once approved, the minutes are finalized and forwarded to the HIRB Chair or a designated board member for signature. The signed copy is retained in the HIRB meeting minutes file, and a copy is forwarded to the Institutional Official.

14.4 Development and Approval of HIRB Policies and Procedures

In accordance with Federal regulations, HIRB has written procedures for each of the following:

1. Conducting reviews of new research. (See Section 5.)
 - Conducting reviews of continuing research. (See Section 6.2.) Reporting its findings and actions to investigators and the institution. (See Sections 5.6, 12.4, and 13.5.)
 - Determining which projects require review more often than annually. (See Section 6.3.)
 - Determining which projects need verification from sources other than the investigators that no material changes have occurred since previous HIRB review. (See Sections 2.9 and 6.2.)
 - Ensuring prompt reporting to HIRB of proposed changes in research protocols and ensuring that proposed changes to approved research are not initiated without HIRB review and approval except when necessary to eliminate apparent immediate hazards to the participant(s). (See Section 6.1.)
 - Ensuring prompt reporting to HIRB, appropriate institutional officials, any relevant Federal department or agency head, and OHRP of: (a) any unanticipated problems involving risks to participants or others; (b) any serious or continuing noncompliance with Federal regulations or the requirements or determinations of HIRB; and (c) any suspension or termination of HIRB approval. (See Sections 12 and 13.)

Written HIRB procedures include step-by-step descriptions with key operational details for each of the above procedures, including:

1. A description of the primary reviewer system used for new applications for research projects, progress reports for continuing review, requests for amendments and changes, reports of unanticipated problems, and reports and allegations of serious or continuing noncompliance.
 - Lists of specific documents distributed to primary reviewers and, if applicable, to all other HIRB members for review of new applications for research projects, progress reports for continuing review, requests for amendments and changes, reports of unanticipated problems, and reports and allegations of serious or continuing noncompliance.
 - Details of any process, such as a subcommittee procedure, that may be used to supplement HIRB's review of new applications for research projects, progress reports for continuing review, requests for amendments and changes, reports of unanticipated problems, and reports and allegations of serious or continuing noncompliance.
 - The timing of document distribution prior to HIRB meetings.
 - The range of possible actions taken by HIRB for protocols undergoing initial or continuing review and protocol changes undergoing review.

- A description of how expedited review is conducted and how expedited approval actions are communicated to HIRB members.
- A description of the procedures for (a) communicating to investigators HIRB actions regarding proposed research and any modifications or clarifications required by HIRB and (b) reviewing and acting upon investigators' responses.
- A description of which institutional official(s) and office(s) are notified of HIRB findings and actions and how this is accomplished.
- A description, if applicable, of which institutional official(s) and office(s) are responsible for further review and approval or disapproval of research that is approved by HIRB.

Note: In accordance with Federal regulations [45 CFR 46.112], no other institutional office or official may approve research that has not been approved by HIRB.

- A procedure specifying how HIRB determines which protocols require review more often than annually, including the specific criteria used to make these determinations.
- A specific procedure for how HIRB determines which projects need verification from sources other than the investigators that no material changes have occurred since prior HIRB review, including specific criteria used to make these determinations.
- A description of what steps are taken to ensure that investigators do not implement any protocol changes without prior HIRB review and approval, except when necessary to eliminate apparent immediate hazards to participants.
- A description of the individuals and institutional offices that are responsible for promptly reporting to HIRB, other appropriate institutional officials, supporting Federal agency or department heads, and OHRP any (a) unanticipated problems involving risks to participants or others; (b) any serious or continuing noncompliance with Federal regulations, HIRB policies and procedures, or HIRB determinations; and (c) any suspension or termination of HIRB approval.
- A description of the required time frame for accomplishing the reporting requirements in point #13.
- The range of possible actions taken by HIRB in response to reports of unanticipated problems and reports and allegations of serious or continuing noncompliance.

HIRB policies and procedures are developed and maintained by the HIRB Director and subject to the approval of the HIRB Chair. The HIRB board also may be asked to review proposed new and modified policies and procedures.

At least every three years, the HIRB Director and staff will conduct a thorough review of HIRB policies and procedures and develop and propose needed alterations and additions. The HIRB Director and staff also will frequently monitor the OHRP Web site for the issuance of guidance documents, determination letters, and changes in Federal regulations that may affect HIRB policies and procedures, and the HIRB Director or staff will draft new or revised policies and procedures accordingly. Investigators will be advised of all approved new and modified policies and procedures

via the HIRB Web site and updates to the HIRB Investigator's Manual and HIRB Standard Operating Policies & Procedures.

The HIRB Chair, board members, Director, and staff members are charged with the implementation and enforcement of HIRB policies and procedures.

Applicable Regulations & Guidelines

21 CFR 56.104

45 CFR 46.101, 46.103(b)(4) & (5), 46.108, 46.110, 46.111, & 46.115(a)(2)

OHRP (July 10, 2002). *Compliance Activities: Common Findings and Guidance*.
[<http://www.hhs.gov/ohrp/compliance/findings.pdf>]

OHRP (January 6, 2005). *Federalwide Assurance (FWA) for the Protection of Human Subjects*.
[<http://www.hhs.gov/ohrp/humansubjects/assurance/filasurt.htm>]

OHRP (July 11, 2002). *Guidance on Continuing Review*.
[<http://www.hhs.gov/ohrp/humansubjects/guidance/contrev2002.htm#WHAT%20CONSTITUTES%20SUBSTANTIVE%20AND%20MEANINGFUL>]

OHRP (March 28, 2000). *Guidance on IRB Meetings Convened via Telephone Conference Call*.
[<http://www.hhs.gov/ohrp/references/irbtel.pdf>]

OHRP (July 11, 2002). *Guidance on Written IRB Procedures*.
[<http://www.hhs.gov/ohrp/humansubjects/guidance/irbgd702.htm>]

Homewood Institutional Review Board

Standard Operating Policies & Procedures

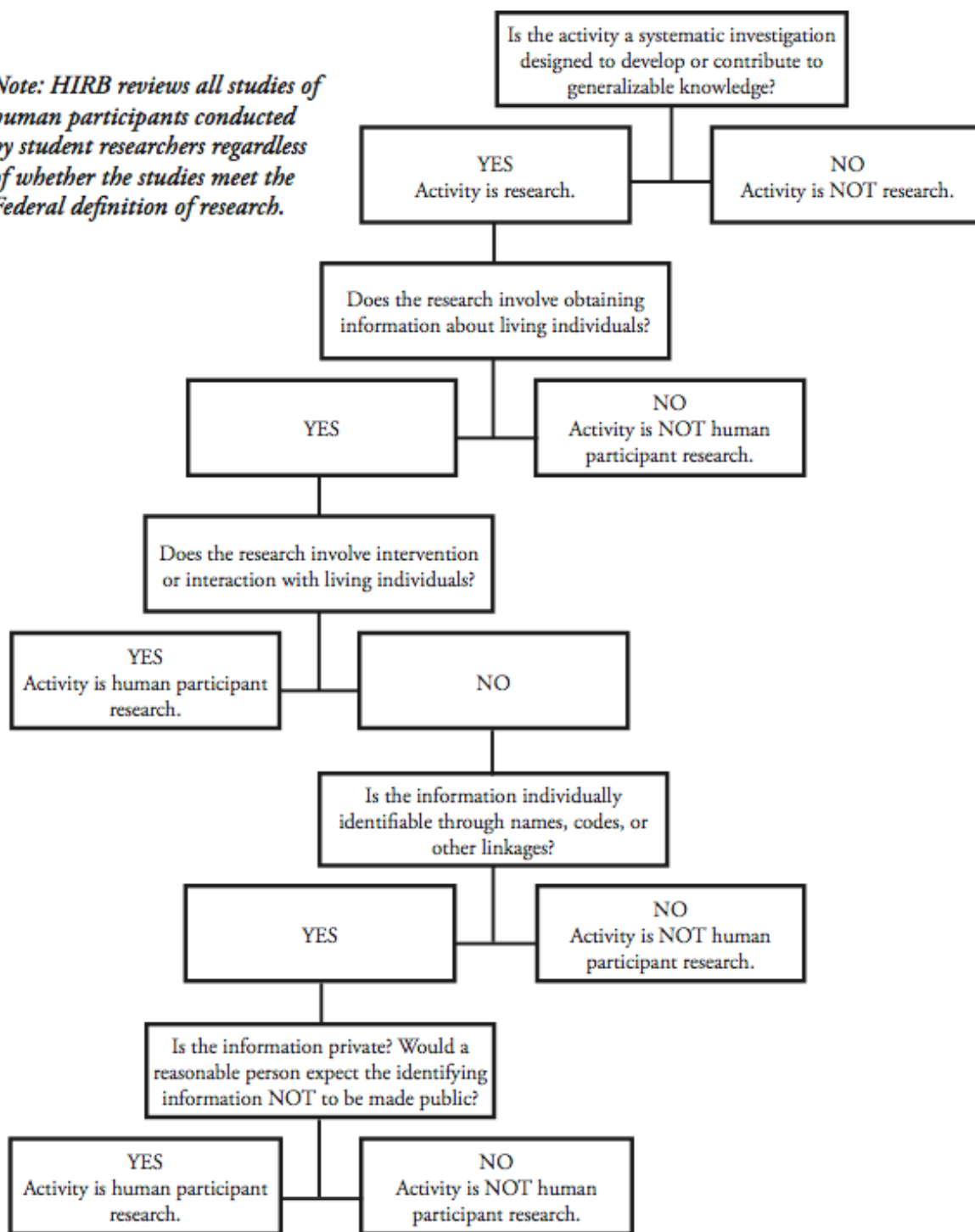
Appendix A: Flow Charts
Date of Revision: 9/22/10

- Chart 1: Is It Human Participant Research, as Defined by Federal Regulations?
- Chart 2: Is the Study Eligible for Exemption?
- Chart 3: Does Exempt Category 1 (for Educational Settings) Apply?
- Chart 4: Do Exempt Categories 2 & 3 (for Ed. Measures and Public Observations) Apply?
- Chart 5: Does Exempt Category 4 (for Existing Data and Specimens) Apply?
- Chart 6: Does Exempt Category 5 (for Public Benefit or Service Programs) Apply?
- Chart 7: Does Exempt Category 6 (for Food Taste and Acceptance Studies) Apply?
- Chart 8: Is the Study Eligible for Expedited Review?
- Chart 9: Can Informed Consent Requirements Be Waived or Altered?
- Chart 10: Can Documentation of Informed Consent Be Waived?
- Chart 11: Are Secondary Research Participants Involved?
- Chart 12: Is Informed Consent Needed from Secondary Research Participants?

Chart 1. Is It Human Participant Research, as Defined by Federal Regulations?

[45 CFR 46]

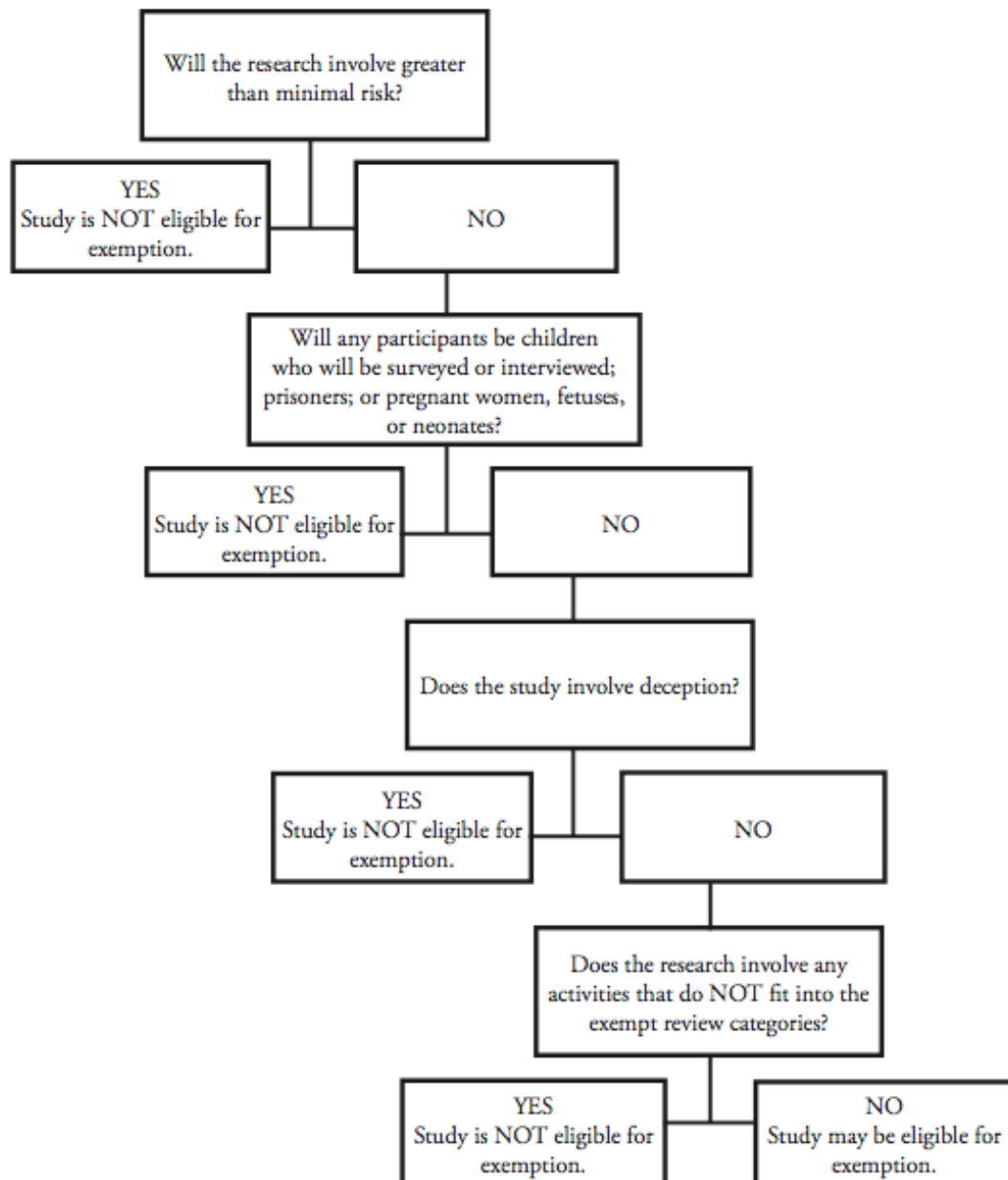
Note: HIRB reviews all studies of human participants conducted by student researchers regardless of whether the studies meet the Federal definition of research.



Note: Investigators should contact the HIRB Office if they have any doubt as to whether their work constitutes human participant research. which must be exempted or approved.

Chart 2. Is the Study Eligible for Exemption?

[45 CFR 46.101(b)]



Note: See Section 5.6 for a list of the exempt review categories. Also see Appendix A Charts 3–7.

Chart 3. Does Exempt Category 1 (Educational Settings) Apply?
[45 CFR 46.101(b)(1)]

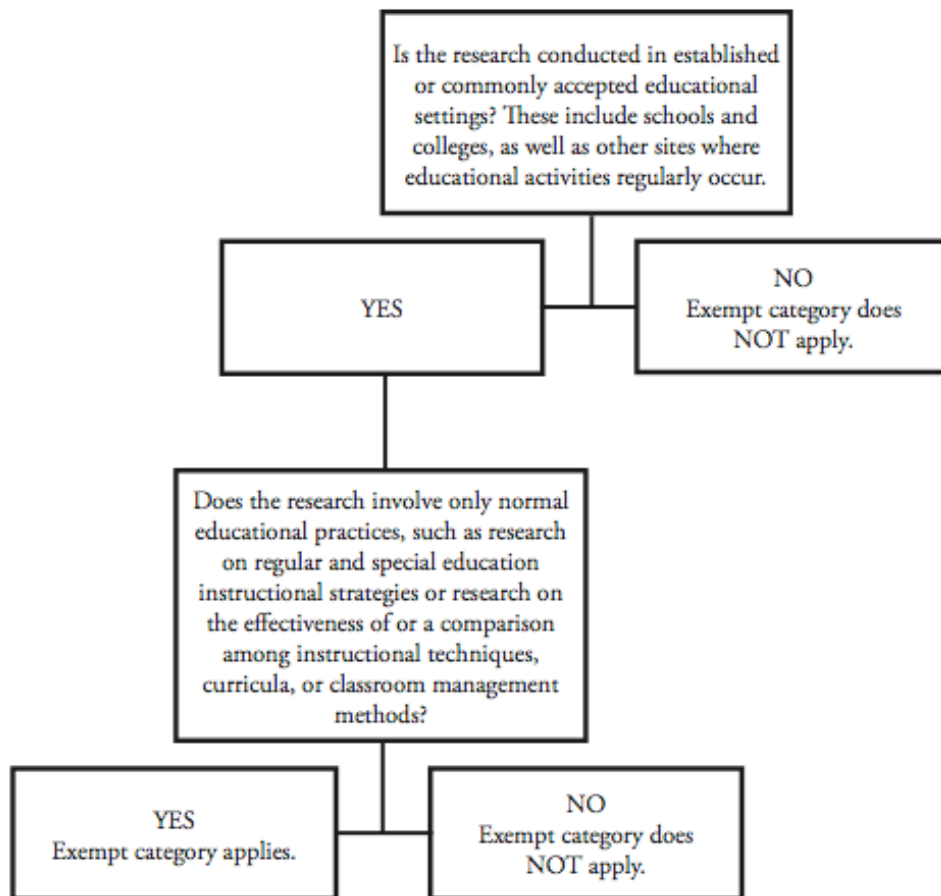


Chart 4. Do Exempt Cats. 2 & 3 (Ed. Tests, Surveys, Interviews, Public Obs.) Apply?
 [45 CFR 46.101(b)(4)]

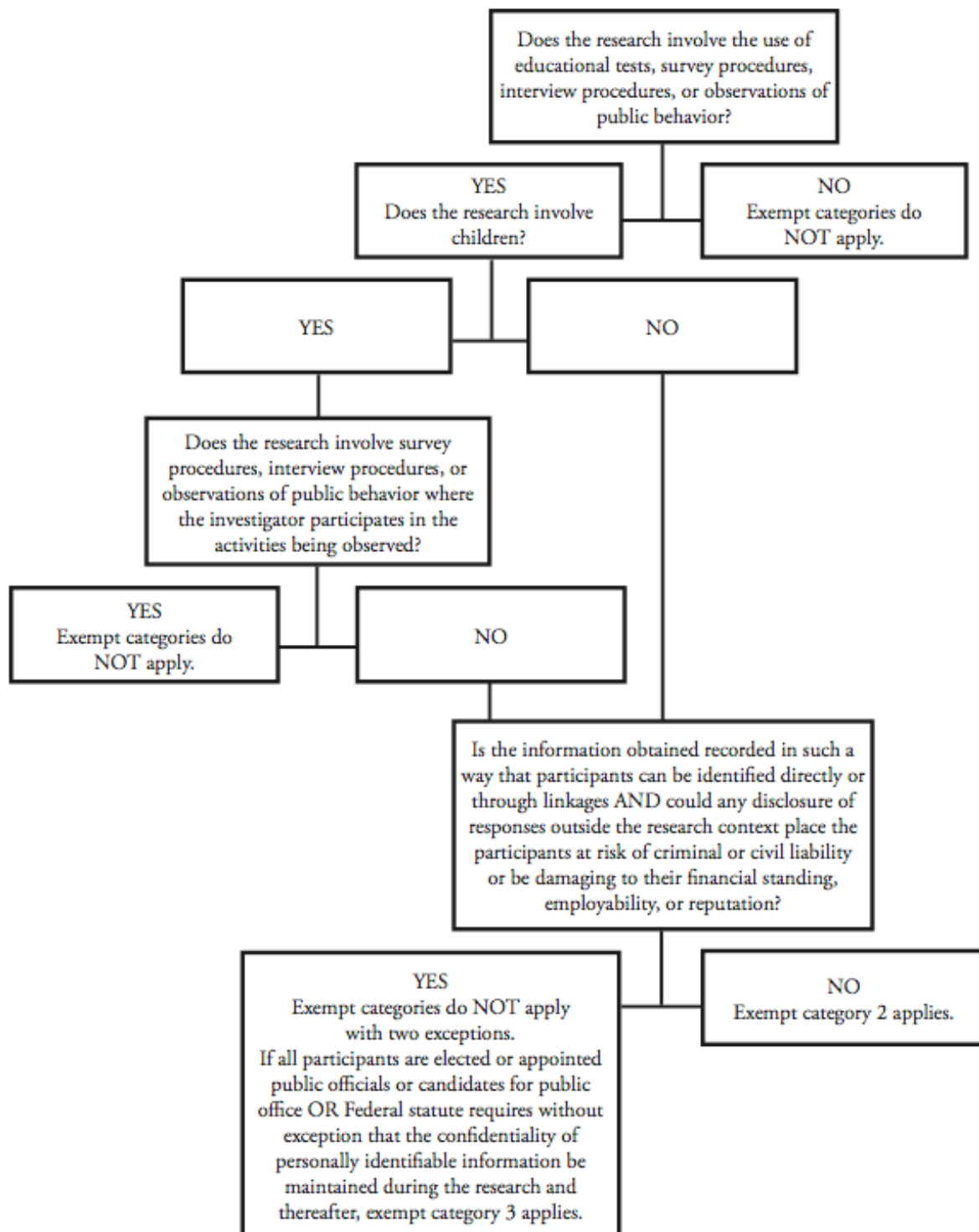


Chart 5. Does Exempt Category 4 (Existing Data and Specimens) Apply?
 [45 CFR 46.101(b)(4)]

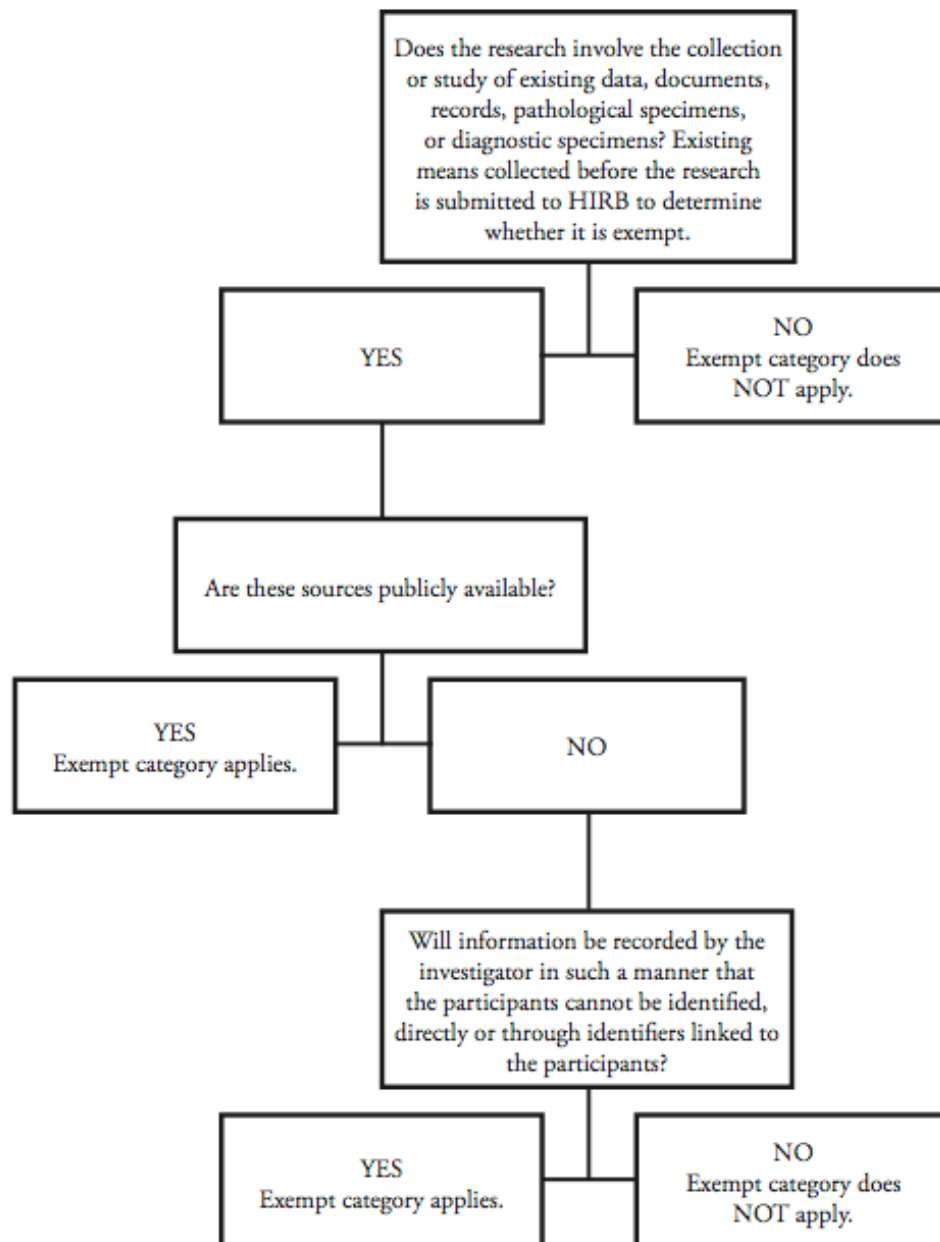


Chart 6. Does Exempt Category 5 (Public Benefit and Service Programs) Apply?
[45 CFR 46.101(b)(5)]

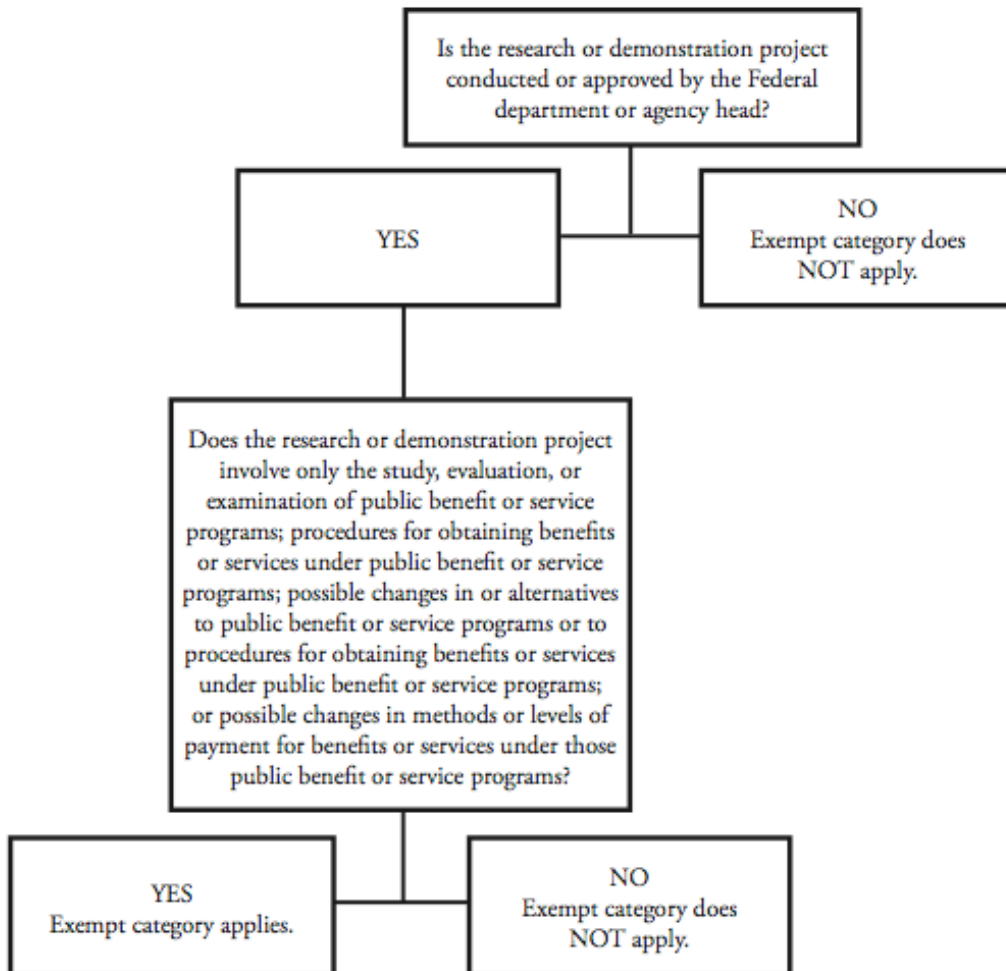


Chart 7. Does Exempt Category 6 (Food Taste and Acceptance Studies) Apply?
 [45 CFR 46.101(b)(6)]

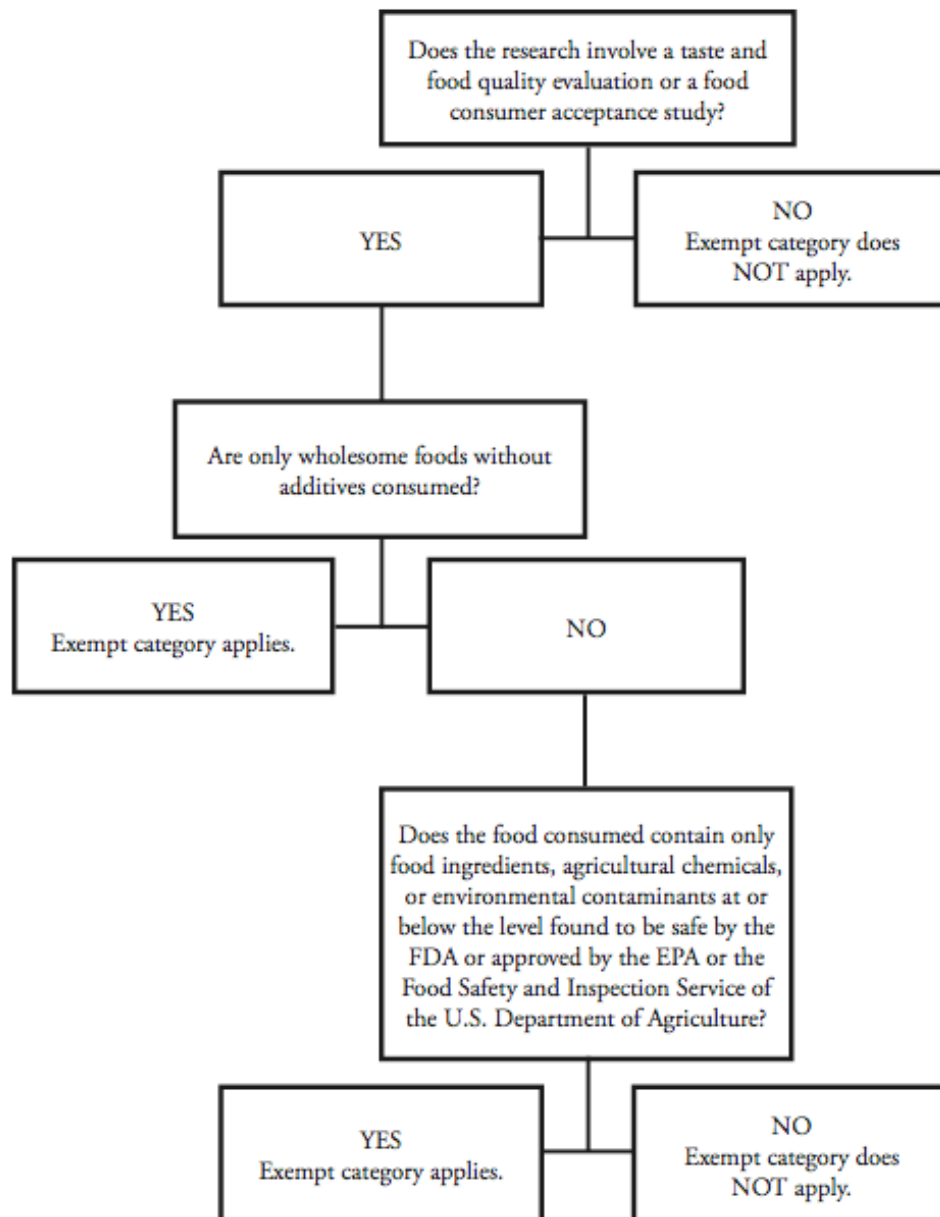


Chart 8. Is the Study Eligible for Expedited Review?

[45 CFR 46.110]

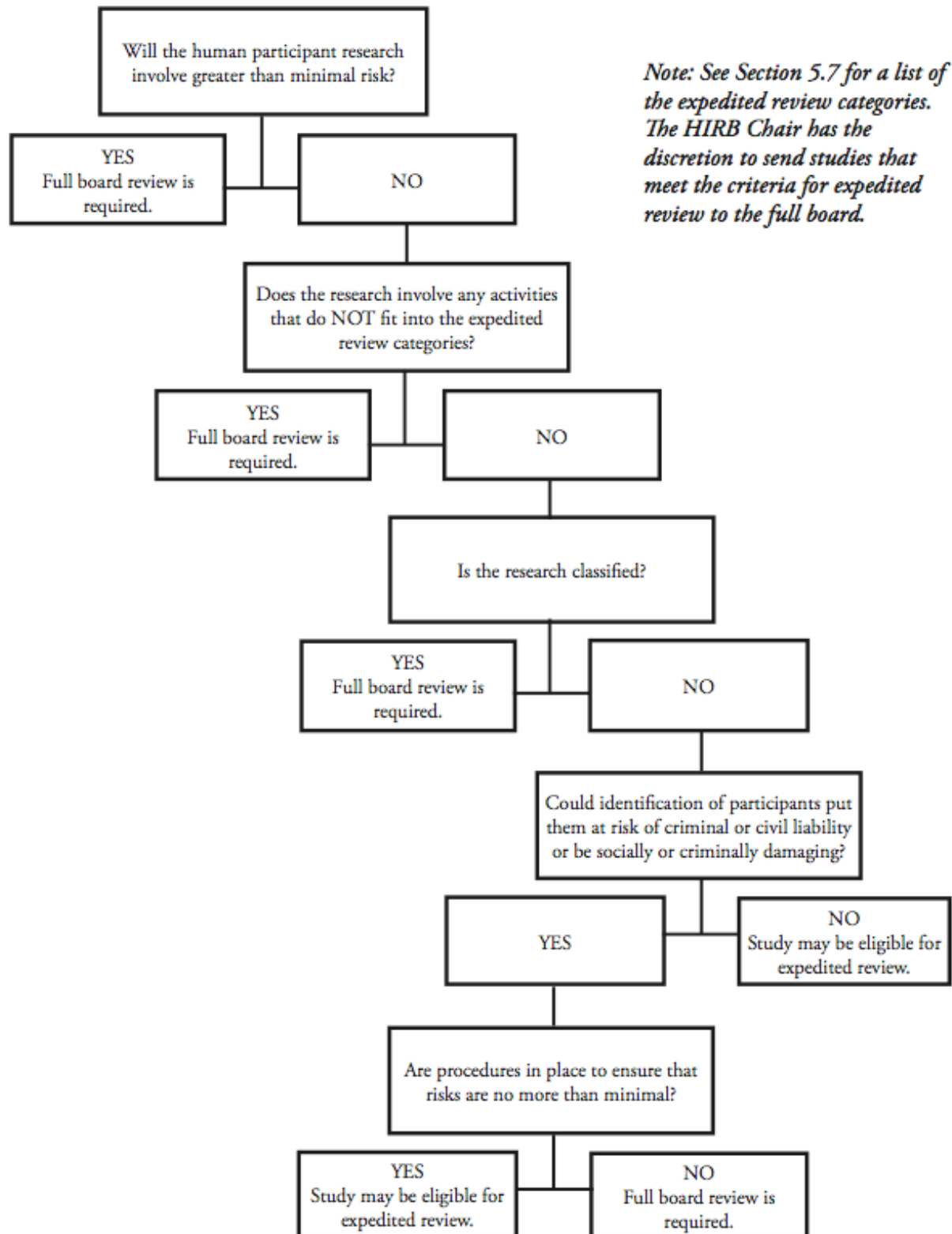
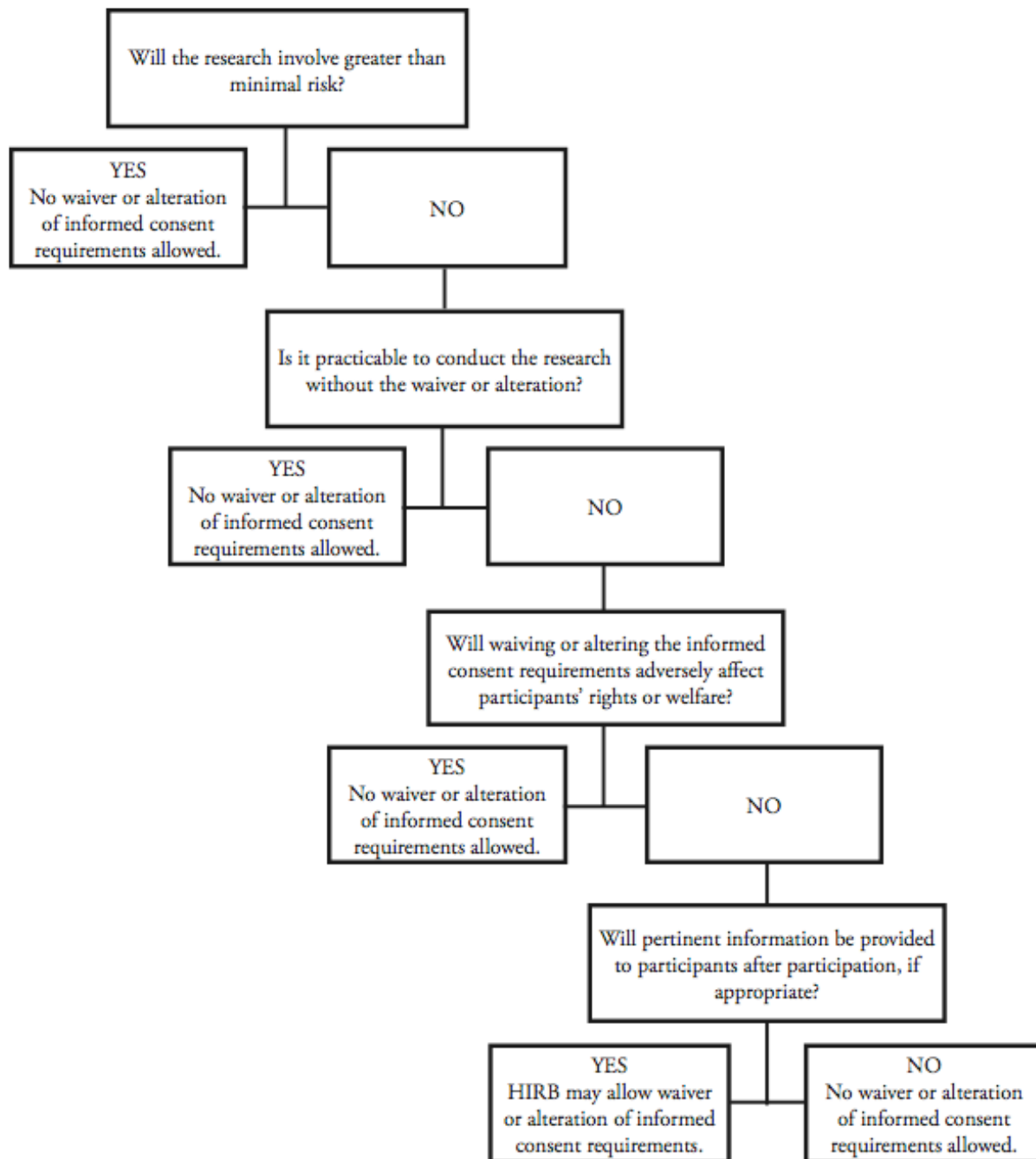


Chart 9. Can Informed Consent Requirements Be Waived or Altered?

[45 CFR 46.101(c & d)]



Note: If participants include children, an alternative provision for waiver of parental permission [45 CFR 408(c)] might apply. See Sections 8.3 and 8.7.

Chart 10. Can Documentation of Informed Consent Be Waived?

[45 CFR 46.117(c)]

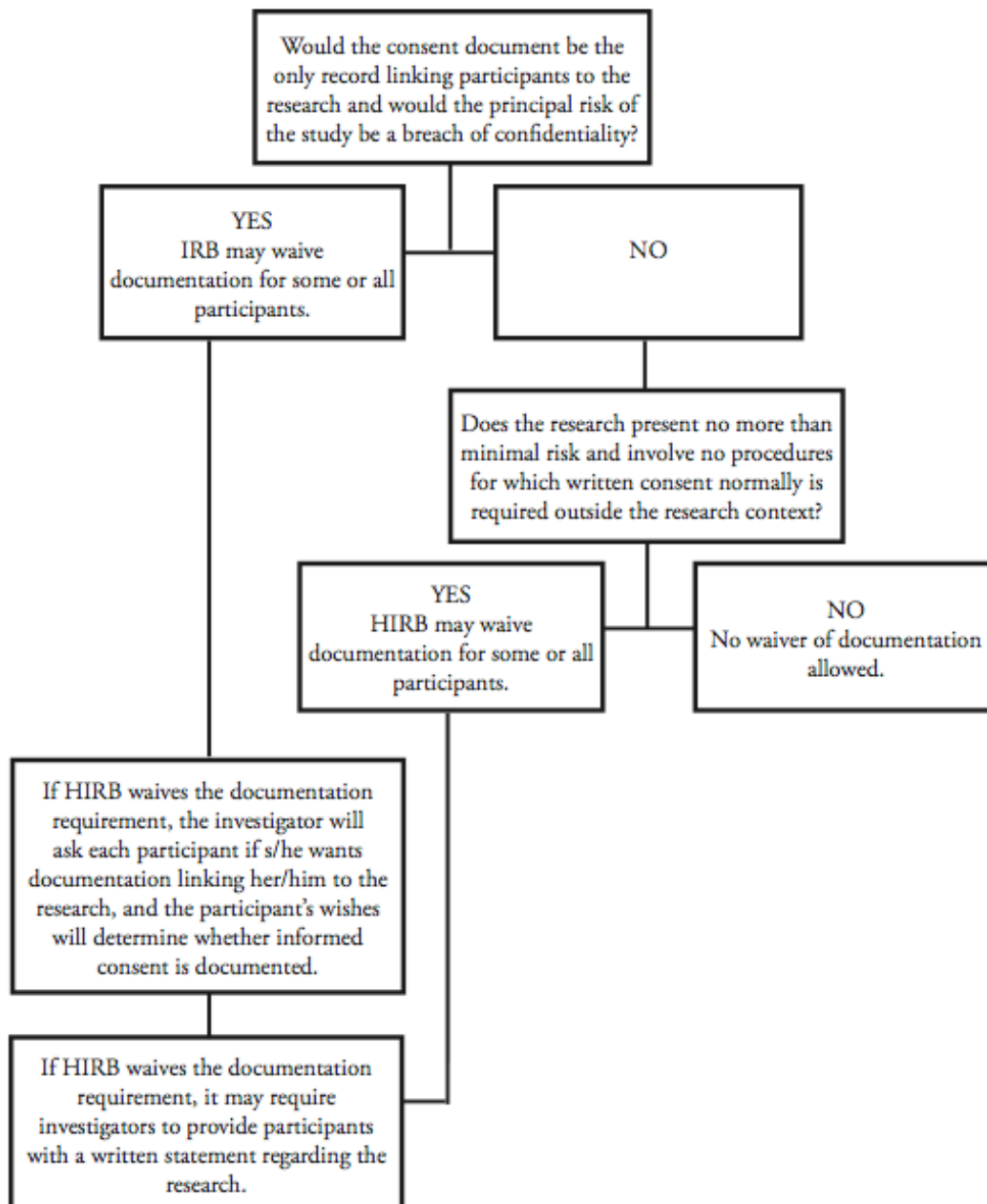


Chart 11. Are Secondary Research Participants Involved?

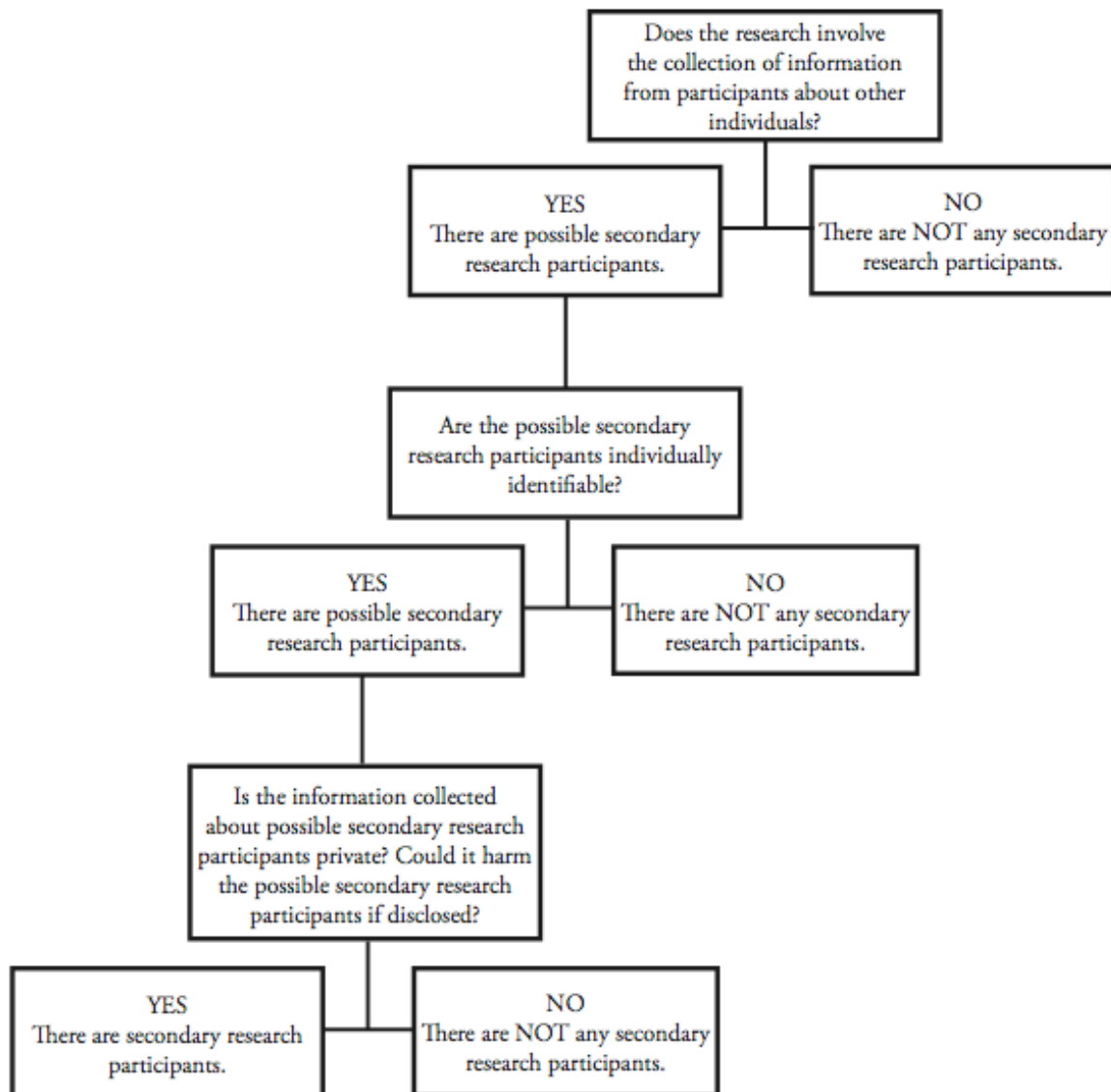
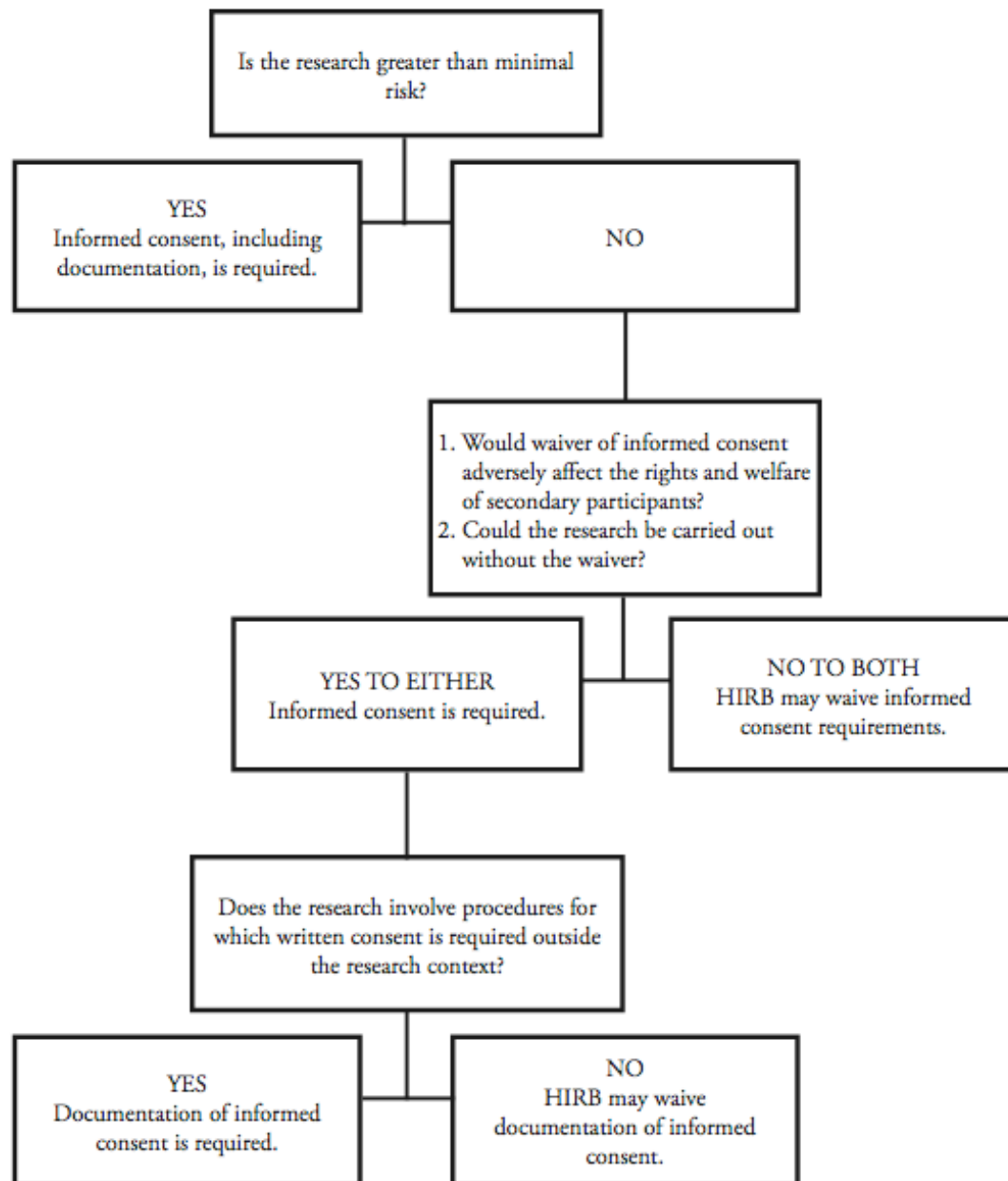


Chart 12. Is Informed Consent Needed from Secondary Research Participants?



Note: If the consent document is the only link between the participant and the research AND the principle risk is the potential harm from a breach of confidentiality, then HIRB may waive documentation of informed consent.