**JHSPH IRB POLICIES**

**UPDATED AND APPROVED 22Nov2019**

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**Acronyms**

CFR: Code of Federal Regulations

CITI: Collaborative Institutional Training Initiative

CRRC: Clinical Radiation Research Committee

CLIA: Clinical Laboratory Improvement Amendment

COI: Conflict of Interest

DHHS: Department of Health and Human Services

DSMB: Data Safety Monitoring Board

DUCI: Drugs Used in Clinical Investigation

FDA: Food and Drug Administration

FWA: Federal Wide Assurance

GCP: Good Clinical Practice

HIPAA: Health Insurance Portability and Accountability Act

HRPP: Human Research Protection Program

IBC: Institutional Biosafety Committee

IDE: Investigational Device Exemption

IDDS: Investigational Drug Data Sheet

IDS: Investigational Drug Service

IND: Investigational New Drug

IO: Institutional Official

IRB: Institutional Review Board

JHHS: Johns Hopkins Health System

JHM: Johns Hopkins Medicine

KKI: Kennedy Krieger Institute

MPH: Masters in Public Health

NHSR: Not Human Subjects Research

NR: Not Research

OGC: Office of General Counsel (JHU)

OHRP: Office of Human Research Protection

PHI: Protected Health Information

PI: Principal Investigator

PRA: Prospective Reimbursement Analysis

P&T: Pharmacy & Therapeutics

RDRC: Radioactive Drug Research Committee

SKCCC: Sidney Kimmel Comprehensive Cancer Center

## Policy No. 101.02 - Disclosure of Research Lab Test Results

If a human subjects research activity includes laboratory testing of blood or other biospecimens collected from study participants, the participants must be informed as to whether the results of those tests will be disclosed to them or their primary care providers. Investigators who process such specimens in the U.S. will comply with Clinical Laboratory Improvement Act (CLIA) requirements and, if processed in Maryland, Maryland State law applicable to laboratory testing. Interpretation of the requirements to meet CLIA standards and State law are made by the Johns Hopkins Bloomberg School of Public Health Institutional Review Board (JHSPH IRB) in consultation with the Johns Hopkins University (JHU) Office of General Counsels (OGC). Under the current interpretation of these requirements, investigators may not report results of diagnostic tests when such tests have been performed in U.S. laboratories that have not been CLIA-certified and do not have a state laboratory license. The IRB may approve a request on a case-by-case basis to allow all participants to receive a form letter indicating that clinical testing is available outside the study and they may wish to have testing conducted at a certified clinical laboratory.

Investigators performing research lab tests on biospecimens should anticipate and include in their consent processes and other communications with study participants the possibility of incidental and secondary findings resulting from these tests. Investigators should make clear under what circumstances those findings may be disclosed to participants.

Disclosure of laboratory testing conducted outside of the United States will be permitted if the testing is performed in laboratories that meet national standards where the lab is located, or international validation standards.

## Policy No. 101.03 - IRB Review of Human Subjects Research

The JHSPH IRB must review and approve all human research projects in which JHSPH is engaged prior to initiation. Under the federal Office of Human Research Protection (OHRP) guidance, and institution is “engaged” in human subjects research when its employee or agent:

1. Is the direct recipient of a U.S. government research grant or contract;
2. Performs invasive or non-invasive procedures for research purposes;
3. Manipulates the environment around a participant for research purposes;
4. Obtains informed consent from a research participant; or
5. Obtains from any source identifiable private information or identifiable biospecimens for research purposes.

See: <http://www.hhs.gov/ohrp/policy/engge08.html>.

“Human research” means any activity that under the DHHS regulations represents “research [[1]](http://irb.jhmi.edu/Policies/102_1.html#f1%23f1)” that involves “human subjects [[2]](http://irb.jhmi.edu/Policies/102_1.html#f2%23f2) ,” or any activity that under FDA regulations represents “research[[3]](http://irb.jhmi.edu/Policies/102_1.html#f3%23f3) ” that involves “human subjects[[4]](http://irb.jhmi.edu/Policies/102_1.html#f4%23f4) ”.

JHSPH faculty investigators are generally not required to seek a determination from the JHSPH IRB as to whether a proposed activity constitutes human subjects research (HSR) when the activity falls outside DHHS and FDA definitions of “research”, but the JHSPH IRB will provide documentation of the Not Human Subjects Research (NHSR) determination for all submissions that meet this definition. One exception involves projects that may qualify as “public health surveillance” activities as defined under 45 CFR 46.102(l)(2). The determination that these activities are not HSR must be made by the JHSPH IRB.

\* \* \* \* \* \* \* \*

[1] Under the DHHS regulations “research” means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. 45 CFR 46.102(l)

[2] Under the DHHS regulations “human subject” means “a living individual about whom an investigator (whether professional or student) conducting research:

(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

(ii) Obtains, uses, studies, analyzes or generates identifiable private information or identifiable biospecimens.” 45 CFR 46 102 (e)

[3] Under the FDA regulations “research” means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part. 21 CFR 50.3(c) and 21 CFR 56.102(c) (Note: Activities are subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the FDC act when they involve any use of a drug or medical device other than the use of an approved drug or device in the course of medical practice)

[4] Under the FDA regulations “human subject” means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient. 21 CFR 50.3(g) and 21 CFR 56.102(e). For clinical investigations involving medical devices, the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit, human subject also means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease.

Note: Research involving deceased individuals is NHSR, but if the identifiable data originate from a HIPAA “covered entity”, HIPAA protects those data until fifty years after the date of death. JHSPH IRB is the HIPAA Privacy Board that will review these projects.

## Policy No. 101.04 - Public Health Practice and Public Health Research

Activities that are performed by JHSPH faculty, staff, and students in the design, implementation, and/or evaluation of public health and health service delivery programs can be, from a regulatory perspective, either “public health practice” or “human subjects research” depending on certain characteristics. (For the purposes of this policy, “public health research” and “human subjects research” are the same.) The JHSPH IRB is authorized to make determinations of practice vs. research as part of its initial review of

a new protocol.

The most fundamental criterion distinguishing practice from research is the primary intent of the activities. As defined by the Common Rule in 45 CFR 46, “research” means "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." The JHSPH IRB will use the faculty’s description of the proposed activities, with particular attention to the articulated intent of the activities, as the primary evidence driving its determination of practice vs. research.

## Policy No. 102.01 - “Not Human Subjects Research” Activities

The federal regulations at 45 CFR 46.102(f) define a “human subject” to be a “living individual about whom an investigator…obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.” There are several types of projects which do not meet the criteria for “human subjects research” and do not require IRB oversight, including:

1. Projects for which the JHSPH investigator is not a direct U.S. grant recipient and provides technical advice (study design, training, instrument development, etc.) to the study investigators, and has no direct contact with study participants or their identifiable private information or identifiable biospecimens;

2. Projects for which the JHSPH investigator may communicate the results to the sponsor or entity under study, but has no intent to publish, present, or otherwise disseminate the study results;

3. Secondary data analysis of de-linked, de-identified data and the investigator had no role in its original collection;

4. Use of information about deceased individuals (but if the data are Protected

Health Information, HIPAA protections attach); and

5. Key informant interviews when the data collected is FROM the informant, but not

ABOUT the informant. If the risk to informants is more than minimal, the JHSPH IRB may serve in an advisory capacity to the Institutional Official.

## Policy No. 102.02 - Course-Sponsored Human Subjects Research Projects – for Educational Purposes Only

Some JHSPH courses designed to teach or use methodology of human subjects research involve student projects which are designed to obtain private information from human subjects. The results of these projects will not be “generalized”; they will not be published or otherwise broadly disseminated. These projects do not meet the regulatory definition of “human subjects research”, but the institution requires the projects to apply the same ethical standards as are required for human subjects research projects reviewed and approved by the JHSPH IRB.

Faculty teaching courses that include human subjects research methodology and exercises that will involve members of the community must follow guidance provided in the “[Guidelines for use of surveys, interviews or other forms of data collection in JHSPH courses](https://www.jhsph.edu/offices-and-services/institutional-review-board/_pdfs-and-docs/Guidelines%20for%20use%20of%20Surveys%20Interviews%20or%20other%20Forms%20of%20Data%20Collection%20in%20JHSPH%20Courses.pdf)” developed by the dean’s office**.** If the data collected may be disseminated beyond the confines of the institution, a new research application may be required.

## Policy No. 102.03 – Student-Initiated “Not Research” Projects Involving Human Participants: Internal Presentations Do Not Contribute to “Generalizable Knowledge”

Under the federal regulations which govern human subjects research, “research” is defined as “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge” (45 CFR

46.102(d)). “Generalizability” refers to dissemination of research results such that others may assess those results and determine whether they have potential for application beyond the source study setting. In academic institutions like the JHSPH, a student-initiated research project involving the collection of, or use of, private information from human participants, may be an element of a degree program (e.g., the MPH Capstone). However, the outcome of the project will be presented only

in a JHSPH school-based setting, not in a broader media. We consider the presentation of student-initiated research project outcomes in an internal setting to be part of the educational mandate, and not “designed to develop or contribute to generalizable knowledge.” The JHSPH IRB will determine such projects to be “not research” (NR). Of course, all ethical principles associated with research interactions with human participants will govern such projects, and review may be required by the Practicum Review Board.

## Policy No. 103.01 - Human Subjects Protection Program

The President of The Johns Hopkins University (JHU) has delegated authority to develop, implement, and monitor all human subjects protection programs (HSPP) to the Deans of the Divisions of the University, including the JHSPH. The Dean of the JHSPH has delegated this authority to an Institutional Official (IO), the Vice Dean for Research. The IO has the authority and independence to ensure implementation and maintenance of the HSPP and JHSPH IRB structure and function. See: [JHU Policy on Institutional Review Board Authority](https://policies.jhu.edu/?event=render&mid=768&pid=32374&fid=policy_32374.pdf&_=0.207128773256).

The IO will be responsible for the registering and maintaining the JHSPH Federal Wide Assurance (FWA) with the OHRP, for generating and implementing all institutional human subjects research policies, and for oversight of the IRB office.

## Policy No. 103.02 - Student Investigators and Post-Doctoral Trainees

JHSPH students and post-doctoral trainees (“students”) may not serve as principal investigator for human subjects research projects. A student investigator who is undertaking a research project in partial fulfillment of the requirements of his or her degree program or for other educational reasons, and has a faculty advisor to supervise the process and take ultimate responsibility for the conduct of the study. In this situation, the PI must provide to the IRB details about the oversight of the student investigator’s activities. The JHSPH IRB must review all such studies, including studies supervised by a PI from an external institution. A student may also serve as a study team member performing routine staff duties like record keeping, data collection or analysis, or lab work. Whatever the role, the student has the same compliance training requirements that any other research team member must provide.

In order to ensure that all student-initiated projects receive appropriate review, such projects must be submitted to the IRB for a determination as to whether they qualify as “Not Research” (NR), “Not Human Subjects Research” (NHSR), “Human Subjects Research (HSR) Exempt from IRB Review”, or HSR requiring IRB review. The IRB office will provide the student guidance on this process and documentation of its determination.

Undergraduate Students

In considering the appropriateness of JHSPH faculty supervision of undergraduates who are interested in research, it is useful to make a distinction between research projects that are being conducted by a JHSPH faculty member and those that are initiated by the student. The key aspect of the distinction involves maintaining JHSPH IRB’s standard for faculty oversight of research activities, particularly those in international locales.

Undergraduates who serve as study team members for ongoing, **faculty-initiated**, human subjects research projects are subject to the same JHSPH IRB requirements as other comparable study team members. The decision to add them to an existing IRB protocol is subject to existing criteria.

With respect to student-initiated research that does not fall under the auspices of an existing or in progress JHSPH IRB-approved project, it is unlikely that a JHSPH faculty member can provide sufficient oversight. As such, while a JHSPH faculty member may serve as a technical advisor on such projects based on their content knowledge and willingness to do so, JHSPH faculty members may not serve as Principal Investigators for undergraduate student-initiated human subjects research and such applications may not be processed through the JHSPH IRB. In general, undergraduate projects are overseen by the Homewood IRB.

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## Policy No. 103.03 - JHSPH Assurance of Compliance with DHHS and FDA Regulations

The JHSPH will provide written assurance to the OHRP to comply with the requirement of 45 CFR 46.103. Written assurance will be maintained and renewed in accordance with regulations.

As stated in the Federal Wide Assurance (FWA) on file with OHRP, the JHSPH is guided by the ethical principles stated in the Belmont Report and codified by the Department of Health and Human Services (DHHS) regulations at 45 CFR 46, and the FDA regulations in 21 CFR 50 and 56. The JHSPH adheres to the guidance provided by the OHRP and by the FDA as part of that commitment. The JHSPH IRB will follow institutional policy for studies involving students and employees. This fundamental commitment to the protection of human subjects applies to all human subject research conducted by a JHSPH faculty member, regardless of funding source or site of the research. All projects conducted by JHSPH faculty which meet the definition of research and that involve human subjects will be reviewed by the JHSPH IRB. The JHSPH IRB may enter into IRB reliance agreements, for oversight of non-exempt research, with external institutions that have FWAs. The reliance agreement will document the institution’s reliance on the IRB for oversight of the research and the responsibility that each entity, the relying institution and the reviewing institution, will undertake to ensure compliance with federal regulations. 45 CFR 46.103.(e)

The JHSPH IRB, and any IRB upon which the JHSPH relies to review human subjects research, has the authority to:

* Approve, require modifications to secure approval, or disapprove, all human subjects research activities overseen and conducted by JHSPH.
* Suspend or terminate approval of research that is not being conducted in accordance with IRB requirements or that has been associated with unexpected serious harm to participants.
* Observe, or have a third party observe, the consent process.
* Observe, or have a third party observe, the conduct of the research.

JHSPH IRB Independence

Officials of the JHSPH may not approve research if it has not been approved by the IRB; officials of the JHSPH may disapprove research that has been approved by the IRB.

When an application is submitted for JHSPH IRB review that involves research populations outside the U.S., the IRB may accept the review by the local IRB or Ethics Board to satisfy the local context review requirement. The IRB will request from the JHSPH investigator a copy of the local ethics approval document. If no formal local ethics review committee is available to review, the JHSPH IRB will ask the PI to suggest an alternative proposal to ensure that the local community is represented. If the research is funded by a U.S. government agency that has accepted 45 CFR 46 as its human subjects research regulation, foreign subrecipients of federal dollars must have an FWA and be overseen by an IRB registered with OHRP.

## Policy No. 103.04 - List of IRB Members

The JHSPH shall maintain a list of IRB primary and alternate members for its internal IRBs. IRBs will have at least 5 members and will be diverse in terms of gender and scientific expertise. There will also be at least one member who is non- scientific and one who is unaffiliated with the institution and who has no family member that is affiliated with Hopkins. The list shall include the following information: name; earned degrees; representative capacity; indications of experience (such as board certifications) and employment status of each member. Alternate members shall receive the same membership training as primary members. Alternate members who attend a convened meeting shall be identified in minutes of the meeting. The standard term for IRB membership is 3 years, with an option to renew in some cases. Changes to IRB membership will be reported to the OHRP in a timely fashion.

## Policy No. 103.05 - IRB Meeting Procedures

The Institutional Official (IO), the Director of the JHSPH IRB, and the Chairs of the JHSPH IRBs are responsible for establishing JHSPH IRB meeting procedures. These procedures include preparing the agendas for the meetings, assembling and distributing the meeting packets, selecting the primary reviewer, recording and processing the minutes of the meeting, and communicating with investigators. Convened meetings for all JHSPH IRBs shall occur weekly, unless circumstances dictate a meeting must be cancelled (examples: lack of quorum, University holidays, weather-related changes,

etc.)

The JHSPH IRB meeting will begin when a quorum is present, including a non-scientific member. The Chair will open the meeting and call each application or item of business before the committee. In the event that the Chair is called from the room or leaves early, the meeting may continue so long as a quorum exists.

## Policy No. 103.06 - Reports of Unanticipated Problems Involving Risks to Participants or to Others (Problem/Event Reporting)

The JHSPH requires researchers to comply with all applicable local, state, and federal regulations in the conduct of research studies. As part of this requirement, researchers are required to submit to the JHSPH IRB written reports of events that meet the definition of “unanticipated problems involving risks to participants or to others.”

Principal investigators must report such problems/events to the IRB promptly, as well as to applicable regulatory agencies, sponsors, and institutional officials.

A. “Unanticipated problems involving risks to participants or others” is defined as:

(1) The information is **unexpected** in terms of nature, severity, or frequency, given:

a) the research procedures described in the protocol and informed consent document;

and

b) the characteristics of the subject population being studied; and

(2) The information about the event indicates that participants or others are at **greater risk of harm** (including physical, psychological, economic, or social harm) than was previously known or recognized.

B. “Prompt reporting” is defined to be “as soon as possible after the PI learns of the event”, but in all cases **within 10 working days**.

C. Reportable Problem/Events

The JHSPH PI must promptly report the following unanticipated problems or events:

1. Event (including on-site and off-site adverse event reports, injuries, side effects, breaches of confidentiality, or other problems) that occurs any time during or after the research study, which in the opinion of the PI:

a. involved **harm** to one or more participants or others, or placed one or more participants or others at increased risk of harm;

b. is **unexpected** (an event is “unexpected” when it is not described with specificity in the protocol and informed consent document; or if described with specificity, it occurs beyond the expected frequency and/or severity identified); and

c. is **related** to the research procedures (an event is “related to the research procedures” if in the opinion of the principal investigator, it was more likely than not to be caused by the research procedures.)

2. Information that indicates a change to the risk:benefit ratio of the research. For example:

a. An interim analysis indicates that participants have a lower rate of response to treatment than initially expected

b. Safety monitoring indicates that a particular side effect is more severe, or more frequent than initially expected

c. A paper is published from another study that shows that an arm of the research study is of no therapeutic value

3. Change(s) in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.

4. Change(s) to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant

5. Incarceration of a participant

6. Event that requires prompt reporting to the sponsor

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

8. Protocol “violation” (a term often used by NIH or commercial sponsors, meaning an accidental or unintentional change to the IRB approved protocol) that placed one or more participants at increased risk, or has the potential to occur again

9. An unanticipated adverse device effect as defined by FDA at 21 CFR Part

812.3(s).

Events labeled as “reportable events” in research involving investigational drugs or devices may or may not meet the definition of an “unanticipated problem.” In such cases, the PI must report the event to the JHSPH IRB if it meets the definition of an unanticipated problem or if a sponsor or regulatory authority requires report to the IRB. Events that the sponsor requires the PI to report, but which do not meet the definition of an “unanticipated problem involving risk to participants or to others” will be acknowledged by the IRB but will not be reviewed by an IRB member.

The JHSPH IRB will review each reported problem/event to determine if it meets the definition of an unanticipated problem involving risks to participants or others. Review of a problem/event may require use of a consultant, or assistance from the division or department chair, to collect additional information before a determination is made.

The JHSPH IRB will authorize appropriate actions to address the problem. The range of actions may be taken by the Institutional Official, other senior JHSPH officials charged with taking action, or the IRB. The JHSPH IRB will inform the IO when a determination has been made that a problem/event meets the definition of an unanticipated problem involving risks to participants or others. The IO will fulfill the requirements to report the action to federal departments or agencies as required by regulation and with JHSPH policy.

## Policy No. 103.07 - Investigator Non-Compliance and Protocol Deviations

The JHSPH IRB may only approve applications that meet the criteria set forth in government regulations, JHSPH policies, and other federal, state, and local law and regulations. IRB approval notices to the PI detail any special conditions or requirements for conduct of the research, and provide a time limit on the approval period. The PI is responsible for conducting the approved research in accord with the IRB’s requirements. If the PI departs from approved study procedures, the PI must report that departure as caused by an “unanticipated problem that posed risk to subjects or others”, or as either an incident of non-compliance, or as a “protocol deviation”.

This policy deals with non-compliance and protocol deviations. A companion policy,

103.06 “Reports of Unanticipated Problems Involving Risks to Participants or Others,” deals with unanticipated problems. This policy distinguishes those events from incidents of “investigator non-compliance”, both of which must promptly be reported to the IRB, and from administrative and minor “protocol deviations” which do not require prompt report to the IRB.

This policy clarifies all three possible situations – unanticipated problems, non- compliance, and protocol deviations – and provides explicit guidance on required actions.

Reporting Non-Compliance

There may be different reasons why a PI or study team member decides to depart from approved protocol procedures, and the consequence of that decision will depend upon the circumstances. A departure from the approved protocol that constitutes an “unanticipated problem involving risks to subjects or to others” (see Policy 103.06) or is serious or continuing “non-compliance” must be reported promptly to the IRB using the *Problem/Event Report*, as follows:

**1. Emergency situations:** When a departure from the approved protocol occurs in an *emergency situation***,** such as when it is required to protect the life or physical well- being of a participant, the sponsor and the reviewing IRB must be notified as soon as possible, but in no event later than 5 days after the ***emergency*** occurs. [[21 CFR](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm)

[812.150(a)(4)](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm) .]

**2. Substantive, non-emergency departures without prior approval:** A planned departure from approved procedures that does not involve an emergency situation (e.g., is “non-emergency”) and represents a substantive change in the protocol as approved by the IRB must be submitted as an Amendment. The IRB must approve the request before the proposed change is implemented. If a major, non-emergency departure from approved procedures occurs (either by accident or intent) without prior IRB approval,

the event is considered to be non-compliance. The PI’s failure to report promptly any major, non-emergency departure from approved procedures, for which the PI did not

obtain prior approval, is itself an incident of non-compliance.

Definitions

*Non-compliance (minor, serious, and continuing):*

“Non-compliance” is defined as failure on the part of the PI, any member of the study team, or any individual involved in research review or oversight to:

* follow the terms of JHSPH IRB approval (including the approved Research Plan and Consent Process), or
* abide by applicable laws or regulations or JHSPH policies, including failure to submit research for IRB review and approval prior to commencing research.

“Minor non-compliance” is defined to be reported incidents or events which are not either serious or continuing non-compliance.

“Serious non-compliance” is defined to be failure to comply with laws or regulations, JHSPH policies, or the requirements or determinations of the IRB, when that failure actually or potentially increases risk to participants or adversely affects the rights and welfare of the participants. A single instance of non-compliance may be determined by the IRB to be serious non-compliance (i.e., continuing non-compliance is not a necessary prerequisite of serious non-compliance). The JHSPH IRB is obligated to report incidents of serious non-compliance to the sponsor and to federal authorities.

“Continuing non-compliance” is defined to be a pattern of behavior or minor non- compliance issues (even when none of them rise to serious non-compliance) that, if unaddressed, may compromise the integrity of human research protections applicable to ongoing or future studies. The JHSPH IRB is obligated to report continuing non- compliance to the sponsor and to federal authorities.

*Protocol Deviations:*

The term “protocol deviation” is not defined by either the HHS human subjects regulations ([45 CFR 46](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm)) or the FDA human subjects regulations ([21 CFR 50](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50)). For JHSPH purposes, a protocol deviation is a *minor or administrative* departure (see definitions below) from the protocol procedures approved by the IRB that was made by the PI without prior IRB approval. In this context, “minor or administrative” protocol deviations are defined as those that do not “affect the scientific soundness of the research plan or the rights, safety, or welfare of human subjects.” Examples of minor or administrative deviations could include: follow up visits that occurred outside the

time frame specified in the protocol because of the participant’s schedule, or blood samples obtained at times close to but not precisely at the time points specified in the protocol.

A PI may report all protocol deviations (i.e., an event that meets this definition) with the Continuing Review/Progress Report using the *Protocol Deviation Summary Sheet.*

Note: eligibility exceptions (or eligibility waivers granted by a sponsor) for enrollment of a specific individual who does not meet the inclusion/exclusion criteria in the IRB-approved protocol are not “protocol deviations”. Rather, they are considered to be protocol non-compliance because eligibility require IRB review and approval before a subject who does not meet the approved protocol inclusion/exclusion criteria may be enrolled.

*Unanticipated Problems:*

“Unanticipated problems involving risks to participants or others” is defined by: (1) an event that is unexpected in terms of nature, severity, or frequency, given

a) the research procedures described in the protocol and informed consent document; and

b) the characteristics of the subject population being studied;

and

(2) The information about the event indicates that participants or others are at greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Unanticipated problems and their reporting are handled in Policy 103.06. In the context of the present policy (103.07 Non-Compliance), one type of unanticipated problem is a “protocol violation” (a term often used by NIH or commercial sponsors, meaning an accidental or unintentional change to the IRB approved protocol) that places one or more participants at increased risk, or has the potential to occur again. This type of unanticipated problem is a form of non-compliance, and both 103.06 and 103.07 apply.

IRB Review of Allegations and Reports of Non-Compliance

The IO, IRB or other JHSPH offices or staff may be notified informally or may receive a non-written allegation of non-compliance. An allegation of non-compliance is an assertion by a second party of an incident of non-compliance. The IO or IRB may authorize the JHSPH Compliance Monitor to conduct a fact-finding effort to determine whether the allegation has a basis in fact. An allegation determined to have a basis in fact and to meet the definition of non-compliance must be forwarded to the IRB for review. An allegation determined not to have a basis in fact will be forwarded to the IO for response to the source of the allegation. An allegation for which it is not possible to adequately determine the facts will be forwarded to the IO or other JHSPH officials for a determination on the appropriate mechanism for fact-finding about the allegation.

The IRB will review written reports of non-compliance or allegations of non-compliance that have a basis in fact. Written reports of non-compliance may be originated by a PI, study team, other staff or offices, sponsors, or collaborators. All written reports, regardless of origin, will be reviewed by the IRB at a group discussion (for IRB X) or for IRB FC, a convened meeting. The IRB is authorized to collect additional information before making a determination. The IRB may collect information using a variety of methods, including communicating directly with the PI and/or study team, or require the PI and study team to meet with the IRB to discuss the report. The IRB may request an audit or ask the IO to conduct an investigation.

The IRB may determine the non-compliance reported is non-reportable minor non-compliance, reportable serious non-compliance, or continuing non-compliance. An IRB finding of minor non-compliance may include a determination of what appropriate corrective actions, if any, should be implemented by the PI and study team.

When the IRB determines there has been serious or continuing non-compliance, the IRB will determine what steps must be taken, if any, to protect enrolled participants. The IRB will determine the elements of a corrective action plan to address the non-

compliance and prevent recurrence. An IRB determination of serious non-compliance or continuing non-compliance must be reported to the IO. Reports to the IO will be sent within 30 days of the IRB’s determination of serious or continuing non-compliance.

The IO is authorized to determine whether a corrective action plan recommended by an IRB should include additional measures. The IO is not authorized to change the IRB’s determination of serious or continuing non-compliance. The IO will report the IRB’s determination of serious or continuing non-compliance to the appropriate regulatory agencies (potentially OHRP, FDA, and the sponsor). Whether or not the IRB determines a report to constitute serious or continuing non-compliance, the IO is authorized to take additional action, which may include suspending or terminating the research.

## Policy No. 103.08 - Reporting to OHRP, the FDA, and other Federal Sponsors

The JHSPH has the responsibility to report unanticipated problems involving risk to subjects or others under Policy 103.06, serious or continuing non-compliance under Policy 103.07, and suspension or termination of approved research under Policy

113.01, to the appropriate federal agencies. The IO is authorized as the individual who will submit reports when an IRB has made a determination under the three cited policies. In cases where the JHSPH IRB and IO determine that additional information is required before submitting a final report, a preliminary report may be made to the appropriate officials, supporting federal agency (as applicable), OHRP, and FDA (as applicable), within one month of the IRB’s determination.

Preliminary and final reports will be prepared for review by the IO and the JHU Office of the General Counsels (OGC). The IO will sign the report within 20 days of the agreed upon final revision of the report. The final report will be submitted to the OHRP if the research is conducted, funded, or overseen by DHHS; to FDA, if the research is regulated by FDA; and to other agencies that are signatories to the Common Rule, if the research is conducted, funded or overseen by such agencies.

A copy of the report will be provided to the reviewing IRB, JHURA if the project is funded by an outside sponsor, and the PI. The IO may determine the report should be provided to the Chair of the Department to which the PI is appointed as faculty and to the Dean of the JHSPH. If the event involves unauthorized use, loss, or disclosure of JHM PHI, a copy will be sent to the JHHS HIPAA Privacy Officer.

## Policy No. 103.09 - Amendments to IRB Approved Research

The JHSPH IRB must review and approve proposed changes in approved research prior to initiation of any changes. Changes in research may encompass amendments, addenda, deletions, or revisions to either the research plan or consent document(s), or changes with other documents associated with a study. If, however, a change in research is necessary to eliminate apparent immediate hazards to a research participant, the PI may proceed with the change without prior IRB review. It is the responsibility of the PI to inform the IRB promptly of the change and the IRB must determine if the modified research is consistent with ensuring participants’ continued welfare.

To initiate a change to approved research, the PI must submit an Amendment Application or an Administrative Amendment for the IRB to review. Minor and administrative changes will be reviewed through an expedited review process; all other amendments will be reviewed by an IRB meeting in a convened setting. Changes in research involving drugs, biologics, or CAMs must be reviewed by the designated IRB Pharmacy &Therapeutics (P&T) member for either an expedited review or a convened review. The P&T member may serve the dual role of primary reviewer and P&T reviewer. Changes or modifications reviewed through an expedited review process will be reported periodically to the IRB members. Complete files of the research project will be made available to any member upon request for further review.

The JHSPH IRB conducting review of amendments is authorized to alter the approval period for the research based on degree of risk posed by the change in research or to retain the original approval period granted at initial review. The IRB may require revisions to consent documents and require notification to enrolled participants of approved changes in research that may affect the participants’ decision to continue in the research.

## Policy No. 103.10 - Ancillary Committee Reviews

All required JHU ancillary committee reviews (Conflict of Interest, Prospective Reimbursement Analysis, Institutional Biosafety Committee, Johns Hopkins Community Physicians, Kennedy Krieger Institute, Pharmacy & Therapeutics, Sidney Kimmell Comprehensive Cancer Center, JHM Clinical Departments, JHM High Risk Review Committees, JHM Data Trust, etc.) must be completed before the JHSPH IRB approves a study. The Ancillary Reviewers will provide information about their reviews, and the IRB will include those findings in its deliberation.

For JHSPH studies that will be reviewed by the Western Institutional Review Board (WIRB), ancillary reviews will be completed prior to sending the research application to WIRB.

Certain ancillary reviews, such as that conducted by the Baltimore City Health Department internal ethics committee, will proceed following JHSPH IRB approval of a study.

## Policy No. 103.11 - Conflict of Interest

Each JHSPH investigator must disclose all financial and fiduciary interests that might appear to present a conflict of interest related to research activities. This process is accomplished through the eDisclose platform as well as during the grant submission process. The JHSPH Policies and Procedure memorandum (PPM) Faculty - 4, Conflicts of Interest and Commitment, and PPM Faculty – 10, Interaction with Industry and Outside Interests provides the general guidelines for COI management. The JHSPH IRB office will work with the Vice Dean for Research and Conflict of Interest Committee to ensure that conflicts associated with conduct of human subjects research protocols are identified and reviewed under the relevant policies before JHSPH IRB review is completed. The JHSPH IRB may not take final action on new applications until COI review is complete and management recommendations are finalized. The JHSPH IRB may accept COI management terms and may impose additional restrictions. The JHSPH IRB may not approve a study with a level of conflict of management that is less than that recommended by the COI.

## Policy No. 103.12 - Human Subjects Research Compliance Training

Human Subjects Research Ethics Compliance Training and Certification through the CITI Program, and renewal of certification every 5 years, is required for all JHSPH research investigators who conduct research involving human participants and their research staff. Training is also required for the Institutional Official, the IRB Chairs, IRB members, and IRB management and staff. In addition to named investigators, research staff includes individuals who have direct contact with human subjects, including those involved in survey administration, focus groups, and the consent process. Investigators who access identifiable private information or biospecimens must also complete HSR ethics training. For studies conducted in locales that have limited access to the current required internet-based training, the PI may propose an alternative training program to ensure that all research staff are trained in human subjects research ethics. The JHSPH IRB will accept module-based training from other institutions, and will also consider in-person training conducted by the PI or other senior research staff members. If such in-person training will be used, the PI must submit to the IRB a summary of the topics that the training will include. The IRB will use its discretion to determine whether the information provided is appropriate for training for the specific study under review.

Other training may be required depending upon the type of research conducted, for example HIPAA training for studies that involve Protected Health Information (PHI), or Good Clinical Practice (GCP) training for clinical trials.

## Policy No. 103.13 - Data and Safety Monitoring of JHSPH Studies

All human subjects research submitted to the JHSPH IRB that includes more than minimal risk, generally must include a data and safety monitoring plan that is appropriate to the risk level of the proposed research. The IRB makes the determination as to whether an activity represents minimal risk or more than minimal risk.

In the event that a formal DSMB will be constituted by a federal funding agency or by clinical consortia conducting the protocol, or is required by the IRB, the IRB may determine that a formal DSMB represents sufficient data and safety monitoring oversight. Names of specific members of a DSMB need not be provided to the IRB as long as the DSMB description contains sufficient information about the expertise of the individuals who will be selected to serve on the DSMB.

## Policy No. 103.14 - Faculty Departure from JHSPH

When a faculty member leaves the institution, that person is no longer an “employee or agent” of the institution, and the JHSPH IRB no longer has jurisdiction over that investigator. Although a faculty member may retain an affiliation after leaving, a*djunct* and *associate* titles do not reflect positions that are “employees or agents” of the institution. Faculty members must notify the JHSPH IRB when they are leaving the institution, and must inform the IRB about their transition plans for any actively enrolling research application for which they serve as PI, and for studies that include identifiable data and/or biospecimens. They may arrange for IRB oversight at their new institution or submit an amendment which transfers PI responsibilities to another JHSPH faculty member.

Departing faculty members should also be aware of the IRB Policy No. 115.02 on Record Retention, and Johns Hopkins University’s data retention and transfer policies.

## Policy No. 103.15 - Visitors to the JHSPH IRB

The JHSPH IRB will permit visitors to attend IRB meetings, with approval of the Chair. In general, visitors include international researchers and ethics committee members, Fogarty scholars, and students from tribal areas that are part of the Center for American Indian Health’s ethics training program. The following procedures must be in place to protect the privacy and confidentiality of deliberations:

* IRB staff should be notified to allow screening of the agenda for items that involve sensitive or privileged information;
* The presence of the visitor should be noted in the minutes; and
* Visitors will be asked to sign a confidentiality statement and will be asked to leave the room for discussions that should only occur in executive session.

Policy No. 103.16 - Institutional Support for the JHSPH IRB  
  
The JHSPH will provide financial and non-financial support for the Human Research Protection Program. Types of support provided shall include sufficient meeting space to support IRB review functions, staff to support IRB functions, IT support for an electronic application system, legal and monitoring expertise, and establishment of a sufficient number of IRBs to efficiently review human research applications.

## Policy No. 103.18 - Policy Development and Communication

The IO has the authority to develop, implement and monitor the Human Research Protection Program (HRPP). The HRPP at JHSPH will be conducted in accordance with federal, state and local law and regulations. The Director of the JHSPH IRB staff will meet on a regular basis with members of the JHU OGC and the IRB Directors from other JHU IRB Offices. They will focus on review of policies and procedures to assure compliance with federal, state, and local laws and regulations and consistency among JHU IRB offices in regulatory and policy interpretation. They will discuss new guidance and alerts from the NIH, OHRP and the FDA, and other information relevant to the HRPP. The meeting will provide an opportunity to address any legal issues associated with the conduct of human subject research at JHSPH, and develop new or amended guidance, policies and/or procedures as needed.

The IO will meet with the Director of the IRB and the Chairs of IRB FC and IRB X on a regular basis to discuss policies, procedures, and guidance, and will seek advice from representatives of the OGC. The IO has the authority to issue policy, guidance, and procedures that govern the HRPP and the associated IRB review processes. Policies will be approved by the IO and noted with the approval date; policies will become effective on the date approved. The IO may delegate authority to approve JHSPH IRB guidance and operating procedures to the Director of the JHSPH IRB or other senior administrative staff as determined appropriate.

## Policy No. 103.19 - Pharmacy & Therapeutics Review

The JHSPH IRB requires review and approval by a representative of the Pharmacy and Therapeutics (P&T) Committee for any use of approved, unlicensed, or unapproved drugs, botanicals, biologics, other related substances (e.g., food additives, food derivatives, vitamins, minerals, extracts, etc.), or complementary and alternative medicines (CAMs) in a research protocol prior to final IRB action on a protocol. This objective will be accomplished by ensuring that IRB FC shall have a member who is also a member of the P&T Committee. When a P&T member for the IRB FC must be absent from a meeting, a P&T Committee alternate may serve as a designated alternate and attend the meeting. In cases where a P&T IRB member or alternate cannot attend a convened meeting, the IRB will postpone review or table applications that include drugs used in clinical investigation until the next meeting when the P&T IRB member can attend.

JHSPH IRB X reviews research that qualifies as a minimal risk activity which may be reviewed through an expedited review process. JHSPH IRB X may review applications that include a marketed drug only if it obtains a written consult from a P&T/IRB member from IRB FC. The P&T IRB members will provide information to the P&T Committees of the JHM hospitals and affiliates to assure proper communication regarding drug research approved for conduct at the Hospitals.

The review process conducted by the P&T IRB Liaison must include review of issues related to the following:

(a) drug safety, including a review of any REMS or black box warnings ;  
(b) drug management;  
(c) study design;  
(d) IND status;  
(e) IDDS review for INDs, and for drugs requested by the P&T representative  
(f) informed consent documents; and  
(g) any other relevant material.

The IRB will be responsible for reviewing [in accord with the Organization policy 103.6(b),] unanticipated problems involving risk, which may include adverse drug events that occur during a clinical investigation.

## Policy No. 103.19a - Drug Use and Control in Clinical Investigation (DUCI)

*Definitions:*

**DUCI (Drug Used in a Clinical Investigation):**  Any drug, biological, botanical, or other substance used for a clinical investigation as named in the investigational protocol/IRB application and a dose, or frequency is specified, or if designated by the P & T IRB liaison.  Such drugs might be either commercially available or not commercially available and used according to, or outside of, the FDA-approved indications.

**Investigational New Drug (IND):**  Any drug or biological product for which the FDA issues an Investigational New Drug (IND) number to allow the drug to be used in a clinical investigation.

**Pharmacy:**  Refers to a pharmacy under the leadership of Johns Hopkins Medicine (JHM).

**IDS pharmacist:**  Refers to a pharmacist in Investigational Drug Services (IDS) at JHM.

**Dispensing Drugs:**  Drug dispensing occurs when a supply of drug that is not patient-specific or that requires manipulation (counting, mixing, preparing, reconstituting, etc.) is given to a study participant.

1. Examples of dispensing drugs include:

* Selecting a quantity of drug from a general bulk supply and placing it in another container for a study participant; or
* Measuring or packaging a drug before giving it to a study participant.

(b) Unless the IRB grants a specific exception, dispensing may only be done by a pharmacist or other practitioner who is licensed/or has a permit to dispense. State and local laws dictate who may dispense medications.

(c) Drugs may only be dispensed upon receipt of a valid order or prescription per the policy of the entity where the research is being conducted. There must always be a retrievable study participant specific record (order or prescription) of the drug being ordered by an authorized prescriber.

**Distributing Drugs: For the purpose of this document,**  a drug is distributed when it is given to the recipient in a pre-labeled container with specific study participant identification (participant’s name or participant- specific identification code), and does not require manipulation (counting, mixing, preparing, etc.) before it is given to the recipient.

(a) Drugs may only be distributed by personnel who have received training about the distribution process and are listed as study team members

(b)  Non-licensed study personnel MAY NOT manipulate drugs within or between containers, may not apply prescription labels to drug containers, or count/confirm counts of study drug. They may transport drugs dispensed by an authorized person to the recipient.

(c)  Drugs may only be distributed after they have been properly dispensed as above and upon receipt of a valid order or prescription per the policy of the entity where the research is being conducted. There must always be a retrievable study participant specific record (order or prescription) of the drug being ordered by an authorized prescriber.

**Administering Drug:** Drug administration occurs when a drug is ingested, injected or enters a study participant through any route of administration.

1. Unless an exception is granted by an IRB P&T liaison, drug administration may only be performed by a person who has a current state license that permits drug administration, or by a person who is credentialed to administer drugs by the entity where the research is being conducted (e.g., nurse, physician, respiratory therapist, nurse practitioner, physician assistant, dentist, podiatrist, or optometrist).
2. Study team members not authorized to administer medications based on the criteria described in (a) above, MAY NOT administer study drugs.

**Storage, Control, Preparation and Dispensing of Drugs Used in Clinical Trials**

Inpatient Studies:

A pharmacy shall store, control, prepare, and dispense all DUCI’s unless a limited exception is granted by the P&T IRB liaison during the IRB application and approval process.

Outpatient Studies:

(a) All outpatient DUCIs requiring manipulation (e.g., mixing, formulating, counting, compounding, etc.) shall be stored, controlled, prepared and dispensed by the pharmacy unless an exception is granted by the P&T IRB liaison during the IRB application and approval process.

(b) In situations where the investigator wishes to store, control, distribute or dispense their own DUCI, such as when a study drug  needs to be dispensed or distributed urgently or the study is conducted at a distant geographic site, the investigator must describe, at the time of IRB application submission, their procedures for performing these functions. Both the P&T IRB liaison and the full IRB committee must approve this arrangement.

**Controlled Substances**

All controlled substances which are used in research must be managed and dispensed by a pharmacy to assure compliance with the Maryland Prescription Drug Monitoring Program and other federal, state, and institutional regulations.

**The Investigational Drug Data Sheet (IDDS)**

(a) An Investigational Drug Data Sheet shall be completed for all IND drugs or when requested by the IRB P&T liaison. The purpose of the IDDS is to provide sufficient information to allow the investigational drug to be dispensed and administered safely.

(b) Completed IDDS shall be reviewed by a P&T IRB liaison as part of the IRB application review process.

(c) Clinicians administering an IND drug shall be familiar with the contents of the IDDS prior to drug administration.  It is the responsibility of the Principal Investigator to assure that the IDDS is available in the patient’s medical record (e.g., research tab of Epic) and/or the clinical area where study drug will be administered.

**Authorization to Prescribe an Investigational Drug**

(a) Principal Investigators shall identify those individuals authorized to prescribe investigational drugs used in their study. For each investigational drug, the completed IDDS shall indicate those authorized to prescribe the investigational drug.

(b) Anyone who dispenses an investigational drug shall verify that the prescriber is authorized to do so prior to dispensing the drug. This can be accomplished by referencing the IDDS.

**Principal Investigator Auditing**

(a) In situations where a JHM investigator has been approved to control a DUCI during the conduct of a JHSPH IRB approved study, an IDS pharmacist may be asked to audit the storage, control, preparation and dispensing of the investigational drug to assure that all regulatory and local institutional requirements are met. The frequency and nature of the audits will be determined by the IRB in consultation with the P & T IRB liaison and the Investigational Drug Service. The P&T IRB liaison in collaboration with the IRB committee will determine how drug control will be audited for studies conducted outside of Johns Hopkins.

(b) Audits of IND studies may be conducted (a) prior to the study beginning, (b) within 1 month of the beginning of patient accrual, (c) within one month of each yearly renewal, and (d) upon termination of the study. If unsatisfactory audit findings are discovered which cannot be resolved during the audit, additional audits shall be scheduled until the identified problems are resolved. If the identified problems cannot be resolved, the audit results shall be forwarded to the IRB, which will determine further actions if necessary.

 (c)  A copy of the audit report will be sent to the Principal Investigator.

 (d) When a Principal Investigator receives a study audit report from a regulatory agency or from a study sponsor (or agent of the sponsor), the PI must provide a copy of the report to the IRB with the Continuing Review/Progress Report Application. If there are significant findings, the PI must provide the copy within 5 working days.

 (e) When a Principal Investigator receives a notice that the FDA wishes to audit/inspect study records, the IRB must be notified before the inspection visit occurs.

## Policy No. 103.20 - Investigational Drug Service (IDS)

The JHSPH requires IDS procedures to protect subjects enrolled in studies involving drugs, biologics, botanicals, complementary and alternative medicines (CAMs) and other substances. The IDS staff has been delegated responsibility for assuring that the receipt, dispensing, and record keeping requirements for investigational drugs conform to JHSPH requirements. The JHSPH IRB staff will share with IDS information regarding investigational drugs used in research protocols. In addition, staff of the IDS will have access to the PHIRST system to facilitate this communication and will report audit results to the JHSPH IRB.

## Policy No. 103.21 - Review of Radiation Procedures

Research conducted by JHSPH investigators using procedures that deliver ionizing radiation to subjects must have additional pre-review before IRB action. This pre-review always includes a review by the JHSPH IRB radiation consultant. For protocols where the procedures are conducted at Johns Hopkins Medical Institution facilities, the JHMI broad scope license to administer ionizing radiation includes a further review requirement applicable to new research protocols or to existing approved protocols that incorporate a change in radiation exposure. This review responsibility has been delegated to the CRRC (Clinical Radiation Research Committee) and its subgroup, the RDRC (Radioactive Drug Research Committee).

Studies submitted to the JHSPH IRB for review that include the use of ionizing radiation require the provision of radiation dosimetry information. JHSPH staff are responsible for initiating IRB radiation consultant, CRRC or RDRC review. Questions/concerns raised in the radiation review are sent to investigators by the JHSPH IRB. The JHSPH IRB will not take final action on an application that involves radiation until the radiation review is complete.

## Policy No. 103.22 - Institutional Biosafety Committee

JHSPH requires that certain human subjects research studies be reviewed and approved by the Institutional Biosafety Committee (IBC).  These studies include those in which investigators wish to introduce recombinant or synthetic nucleic acid molecules (DNA/RNA), potentially infectious agents or pathogens, or biological toxins into human subjects.  IBC approval of such research must precede approval for conduct by a JHSPH IRB.

Additionally, JHSPH requires that individuals who collect and/or ship biological specimens register with the Biosafety Office.  For the purposes of human subjects research, this requirement extends to studies conducted at all Hopkins/Affiliates sites.  Investigators must document satisfaction of this requirement in the PHIRST application prior to final approval by JHSPH IRB.

## Policy No. 103.23 – Documentation Required from Collaborating Sites

For federally funded studies, the JHSPH requires documentation of IRB/Ethics Board reviews from collaborative institutions that they have met appropriate OHRP appropriate assurance requirements. Investigators are required to submit approvals from off-site IRBs/Ethics Committees, as well as any required administrative approvals or permissions for conduct of research by JHSPH researchers at non-Hopkins sites. Local IRB approvals must meet all local laws and requirements. If such documentation is pending, the JHSPH IRB may approve the study with administrative changes. JHSPH IRB staff is responsible for communicating with investigators to assure that documentation is provided before final approval and release of consent documentation.

## Policy No. 103.24 - Principal Investigator

Only faculty on the professorial, scientist, or lecturer tracks with primary affiliations in the JHSPH are eligible to serve as a principal investigator (PI) for research studies that involve human subjects. Exceptions may be granted for affiliated or other faculty members under the discretion of the IO and with the approval of the department chair. As part of its assessment of a research application, the JHSPH IRB will consider the PI’s qualifications and expertise to determine whether the faculty member may serve as PI for a particular research investigation. Once the JHSPH IRB reviews and approves a study involving human participants, the PI is solely responsible for the conduct of the study as described in the research plan, and in compliance with institution policy, federal regulations, and state, local, or international laws. All communications with the IRB concerning the research plan and associated documents, except those which deal with administrative issues, must originate from the PI.

The role of the JHSPH PI may vary, depending upon whether the study described in an application is a single site study, one site in a multi-site study, or is the coordinating center for a multi-site study, and should be explained in the research plan. When appropriate, the PI may include collaborating co-investigators from JHSPH or other institutions and may hire or otherwise include research study staff to assist in the implementation of the study procedures and maintenance of the study records. If the study will be conducted at a non-JHSPH site, a management plan must be provided for ensuring that the study will be conducted as approved by the JHSPH IRB.

Research team members described in each protocol must be qualified to perform the research procedures that they have been assigned. The PI is responsible for assembling a team that has the proper qualifications and documentation of training in human subjects research ethics, Individuals performing medical procedures at Johns Hopkins sites and other study sites must be credentialed to perform those procedures. If Fellows are part of the study team, the PI must adhere to the Hopkins policy regarding involvement of Fellows in clinical research. JHSPH IRB questions regarding credentials will be referred to the appropriate offices for response.

## Policy No. 103.25 - Registration of Clinical Trials and Posting Clinical Trial Consent Forms

The JHSPH requires that all clinical trials shall be registered at <http://www.clinicaltrials.gov>. The definition of a clinical trial for purposes of this policy is, “A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.”  
A "health-related biomedical or behavioral outcome" is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects’ biomedical or behavioral status or quality of life”.

The JHSPH PI should consult with commercial sponsors to assure that posting of a trial is in accord with terms of the study contract.

In addition to posting clinical trials on clinicaltrials.gov, for each federally funded clinical trial, one IRB approved consent form used to enroll participants must be posted on a Federal website after the clinical trial is closed to recruitment and no later than 60 days after the last study visit by any participant. The sponsoring federal agency may permit or require redaction of information from the form prior to posting.

## Policy No. 103.26 - Electronic Submission of Research Applications

The JHSPH IRB Office accepts new research applications from JHSPH faculty members through an electronic (PHIRST) system. Applications must contain a research plan which clearly presents the proposed research protocol, any consent documentation, recruitment materials, grant or contract documents, and all data collection instruments. The PI must provide information about investigational and approved drugs, devices, and other products that participants may ingest or apply to their bodies. If the study involves FDA regulated test articles, the PI must provide sponsor’s protocol, investigational brochure, and the IND or IDE number associated with the investigational product. Unregulated products (dietary supplements, vitamins, foods, etc.) must include package inserts, certificates of analysis, or information about sourcing. Any other IRB approvals associated with the project must be included. Applications may only be submitted by the PI. Information and uploaded documents obtained and reviewed as part of IRB functions are treated as confidential.

The electronic system resides on a secure computer network controlled by JHSPH. Access is controlled by the JHSPH IRB Office and is limited to individuals on a need to know basis. All staff of the JHSPH IRB Office and all IRB members must sign a confidentiality agreement as part of their IRB activities. All non-IRB staff granted access must agree to abide by the confidentiality terms stated when access is granted. The information will not be discussed or disclosed outside of the JHSPH review process. Any confidential information from PHIRST distributed by IRB staff to members is done on the JHSPH secure internal email system.

## Policy No. 103.27 - FDA Regulated Device Research

Research involving medical devices must be reviewed and approved by the JHSPH IRB

before the research may begin. The IRB will determine whether the research represents non-significant risk (NSR) device research or significant risk device research. If NSR, the IRB will determine whether the device is exempt from the IDE regulations under 21 CFR 812.2 (c), or is considered to have an approved IDE application under 21 CFR 812.2 (b). The IRB will record the rationale for an NSR assessment on the review sheet for determinations made at an expedited review session. The IRB will document the NSR determination in the minutes for convened

discussions. Proposals that are determined to represent significant risk device research must be reviewed at a convened meeting and may not proceed without submission of an Investigational Device Exemption (IDE) application to the FDA and subsequent receipt of confirmation of the FDA decision on the application.

The JHSPH requires a monitoring process for receipt, dispensing, and record keeping concerning devices that are studied using an IDE granted by FDA. The monitoring process shall be performed at the direction of the IO.

Researchers who serve as a sponsor/investigator for an IDE research project are required by the JHSPH to follow FDA regulations 21 CFR 812 Subpart C applicable to sponsor responsibilities. Monitoring of these studies will be performed at the direction of the IO.

## Policy No. 104.01 - Exempt Research

The JHSPH requires that all human research projects must be either reviewed and approved by an IRB prior to initiation or be found by an IRB to be exempt from federal regulations. The JHSPH IRB is authorized to make exempt determinations; investigators may not make this determination independently. The JHSPH IRB will apply the federal criteria for exemption (at 45 CFR 46.104(d)) in making its exempt determinations. The research activity may not commence before the IRB makes its determination and has provided documentation of that determination to the investigator.

Subparts B (Pregnant women and fetuses), C (Prisoners) and D (Children) have different rules about the application of exempt determinations. Pregnant women may participate in all categories of exemption. Prisoners may participate in exempt studies only if the research is aimed at a broader population that only incidentally includes prisoners. Children may participate in some research determined to be exempt but not others.

The JHSPH IRB is authorized to determine that proposed research that may qualify for exemption requires limited IRB review, or review through an expedited or convened review process. The reason for expedited or convened review will be documented.

The JHSPH IRB may require periodic progress reports from PIs of Exempt studies to facilitate institutional ethical oversight of the research activity.

## Policy No. 107.01 - IRB Member and IRB Office Staff Qualifications

**JHSPH IRB Members**

The JHSPH IRB follows the Federal regulations, 45 CFR 46.107 and 21 CFR 56.107, that require the Institutional Review Board (IRB) to have at least five members. Those members shall have the following characteristics:

• Varied backgrounds, including: professional expertise; diversity of race, gender, and culture; sensitivity to local community issues and attitudes.

• Ability to ascertain the acceptability of proposed research scientifically, and in accordance with institutional commitments and policies, applicable law, and standards of professional conduct and practice.

• Expertise required to provide the IRB with information not only about specialized areas of research, but also about working with various types of research participants, including vulnerable populations.

At least one member of the IRB must have a primary interest in science; and at least one must have a primary interest that is nonscientific in nature. Each IRB must have at least one member who is not affiliated with Johns Hopkins and who is not part of the immediate family of someone who is affiliated with Johns Hopkins. If non-affiliated members are compensated for their IRB service, that payment does not make them “affiliated” if there is no other connection with the institution. Each JHSPH IRB that reviews studies involving investigational or marketed drugs, biologics, botanicals, complementary or alternative medicines, or gene therapy, will have an appointed member from the P&T committee.

The IO has the authority to appoint Chairs of each IRB and the members and alternate members of the IRBs. The factors that the Institutional Official will consider for the leadership appointments include: academic status and record of leadership; expertise; willingness to commit the time required, experience with IRB and human research protection issues, administrative abilities, and personal capacity to listen and guide multiple opinions expressed in a meeting format. The IRB members with scientific expertise will be selected in consultation with the IRB Chairs and IO. Non-scientific members will be selected based upon recommendations from current and former non-scientific IRB members or other members of the IRB community.

Any IRB member who has a conflict of interest with a matter under IRB review must recuse him or herself from consideration of that issue.

**JHSPH IRB Staff**

The JHSPH IRB staff shall include administrative personnel to manage the processing of the applications to the JHSPH IRB and senior staff to review submissions for regulatory and institutional policy compliance. The Director of the IRB will be responsible for both the operations of the IRB Office and for assisting the Institutional Official with compliance issues. The Director, the IO, and the Chairs of the IRBs will work in executive session to develop policies and procedures to guide the human subject protection program at the JHSPH. This executive committee will also address subject and investigator complaints, and assist with FDA and DHHS inquiries and audits.

## Policy No. 107.02 - Consultants to the IRB

The JHSPH IRB may request the assistance of a consultant in preparing for discussion of a research protocol in accordance with DHHS regulations at [45 CFR 46.107](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.107) and FDA regulations at [21 CFR 56.107](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=56.107). If the IRB does not include a member who has worked with a particular vulnerable population, has the appropriate scientific expertise, or has experience working in a particular part of the world where the proposed research may take place, it may request a consult.

Consultations may be formal requests for written comments or email requests and will be documented in the protocol file. Consultants may not vote with the IRB members and must not have a financial conflict of interest with the matter at hand. If the consultant has other potential conflicts of interest (e.g., is a colleague of the PI or an earlier reviewer) that conflict should be disclosed to the IRB, and the IRB may still take the consultant’s comments into consideration.

## Policy No. 107.03 - Training IRB Members and Chairs

In addition to the human subjects compliance training that the JHSPH IRB requires for

all investigators and staff at JHSPH, each new IRB member, alternate member, or Chair must complete the JHSPH IRB Orientation program, which will be conducted by an existing Chair, IRB Office staff, and the Director of the IRB. JHSPH IRB members will be trained in convened and expedited review regulatory criteria and may not serve as an expedited reviewer until the Chair for their committee determines that they have adequate experience to serve as a reviewer. JHSPH IRB members will be provided with copies of the most recent edition of Robert Amdur’s ***Institutional Review Board Member Handbook.*** Additional training opportunities for IRB Chairs and members may be made available.

The IRB Director will be responsible for communicating new NIH, OHRP, FDA, or other relevant guidance or regulatory changes to the IRB members to keep them informed.

The IO with the assistance of the IRB Director, will facilitate periodic self-assessments of IRB chairs, members, and overall committee function.

The IO will periodically assess the performance of the IRB Director, the Chairs, and individual members. The IO may ask members to evaluate the performance of the Chairs. These assessments may be conducted by survey and/or by personal interview. Any adjustment in committee membership will be determined annually and as needed to fill vacancies. Membership selection shall be nondiscriminatory such that no selection is made on the basis of gender (45 CFR 46.107(b)).

## Policy No. 108.1 - Quorum, Voting Status, Attendance of IRB Members

The JHSPH IRB convened meetings will follow general corporate law guidelines using total board membership when considering quorum and alternate voting. A meeting cannot proceed without a quorum, which is one more than half the total committee membership, and without the presence of at least one non-scientific member. Members may attend IRB meetings via teleconferencing. For example, if the IRB has 12 members, quorum will be 7; if the IRB has 11 members, quorum will be 6. Alternate members may substitute for IRB members who are unable to attend a meeting. Alternates may vote for an identified primary member in the primary member’s absence. The minutes of the convened meetings will identify when an alternate member substitutes for a primary member and votes at the meeting.

Vote Counts and Attendance

Member attendance will be recorded at each meeting and the meeting minutes shall identify any individual who serves as an alternate member for a primary member. The presence of any member “attending” via teleconference will be recorded in the attendance records. Total attendance will be reconciled with the vote counts for accuracy.

Any member who has a personal or financial conflict of interest with a study under review must disclose that conflict prior to the discussion of the study. The conflicted person may answer questions about the study, if appropriate, but must leave the room for the final discussion and the vote on the study.

## Policy No. 109.01 - Delegation of Authority to JHSPH IRB

The IO has authorized the JHSPH IRB to review human subjects research projects conducted by JHSPH faculty. All faculty must submit for JHSPH IRB review any human subjects research project, regardless of funding source (or lack thereof) and/or location at which the research will be conducted. JHSPH IRB approval or exempt determination is required before a project may begin.

All non-exempt human subjects research conducted at JHSPH will be reviewed, prospectively approved, and subject to continuing oversight by the JHSPH IRB, unless determined to be exempt from under JHSPH policy. The review will address all the criteria listed in 45 CFR 46.111 (except for the provisions governing Broad Consent) and 21 CFR 56.111. The IRB will evaluate whether resources are adequate to protect participant’s rights and welfare.

The JHSPH IRB may approve, approve with specific changes (approve with administrative changes), require modification to secure approval (“table”), or disapprove proposals. The IRB may suspend, place restrictions upon, or terminate approval of research activities falling within its jurisdiction that are not being conducted in accordance with JHSPH IRB requirements or which have been associated with unexpected adverse events. The JHSPH IRB may have the consent process, or the research procedures, of any study observed by a third party if the IRB determines that such observation is indicated. The JHSPH IRB may re-evaluate the qualifications of the PI and the study team at any time. The decisions of the IRB shall be conveyed to PIs in writing. The PI will notify any sponsors or other interested parties, such as those involved in multi-center studies, as necessary, of IRB decisions. 45 CFR 46.109(d).

An IRB decision to table or disapprove a study must be conveyed to the PI with an explanation of the reasons for its decision. IRB disapproval must be made at a convened meeting and may not be overruled by any other JHSPH authority. The investigator has the opportunity to respond to that explanation in person or in writing. The IRB’s decision, after reviewing the PI’s response, is final.

## Policy No. 109.02 - IRB Communications to Investigators

Approval Notices and Approval Stamp

The JHSPH IRB will provide its approval of a new application, continuing review/progress report, amendment or other changes in a study in writing to the PI. An approval notice will be on JHSPH IRB letterhead but does not require signature of the chair. Approved consent forms and approved print advertisements for recruiting research study participants must carry the IRB approval stamp unless the IRB waives this requirement. It is acceptable that the advertisements and consent documents carry the stamp of the local collaborator when the research activity occurs at a local site. The IRB approval stamp indicates that the document has been reviewed and approved by the IRB. The stamp is only used on finalized documents.

Disapproval Notices

Disapproval of a research protocol or activities associated with that research will be documented and communicated in writing by means of an IRB Letter of Disapproval, which will be sent to the investigator. The letter must identify what has been disapproved and include the reason that the research was disapproved. All Letters of Disapproval must provide an opportunity for the investigator to address the IRB in person or in writing regarding its action.

## Policy No. 109.03 - Complaints from Research Participants, Study Staff, PIs, or the Community

The JHSPH IRB, as part of the duty to review research applications, will receive and respond to complaints or other communication from research participants, investigators or research staff, or members of the community. These communications may present questions, complaints, or other issues of concern that the IRB must help to resolve. The PI must report promptly complaints that address concerns about the safety and welfare of study participants to the IRB on a Problem Event Report. The PI must report all other complaints through the Continuing Review/Progress Report. If the complaint comes to the IRB office, the IRB office will record all complaints, refer them to the PI, and document the resolution of the complaint.

In the case of Problem Event Reports, and complaints that come to the IRB office and involve potential risks to the safety and welfare of study participants or others, the Director of the IRB, in consultation with the IO and the GCO as needed, will determine whether the issue raised poses risk to human subjects. They will decide if other JHSPH officials should be informed, and what steps should be taken to address the concerns. If necessary, the Director of the IRB will work with the IO to contact the PI for the study to collect all needed information.

## Policy No. 109.04 - Allegations of Undue Influence over the JHSPH IRB

JHSPH IRB review processes, and the implementation of JHSPH IRB policies and procedures, are to be conducted objectively and without undue influence over deliberations or processes. IRB members, IRB staff, investigators, or research participants who believe that an attempt has been made to unduly influence IRB decisions, review processes, or application of policies and procedures may contact the IO, the IRB Director, or IRB staff to report a concern. The IO, or JHSPH IRB Director, or other delegated senior staff members will review reports. Outcome of the review will be documented, the complainant provided with a response, and a corrective action plan instituted if deemed necessary.

## Policy No. 109.05 - Minor and Administrative Changes to Approved Study Instruments

The JHSPH IRB must review all study instruments (survey scripts, questionnaires, interview guides, data collection materials, etc.) before they can be used in a research study. The IRB understands that an approved instrument may need modification once implemented, and will permit the following types of changes to be made without prior IRB review, so long as the PI submits a tracked version of the modified instrument at the time of continuing review:

* Rewording of certain provisions to clarify meaning;
* Correcting grammatical or typographical errors; and

Modification of this sort will be regarded as “minor and administrative” protocol deviations which may be summarized for the IRB as part of the PI’s Continuing Review/Progress Report.

Additions or deletions to approved instruments are not considered to be “minor and administrative” protocol changes and must be submitted to the IRB as part of an Amendment Application prior to implementation.

## Policy No. 109.06 - Continuing Review and Progress Reports

JHSPH IRB will provide continuing review of approved human subjects research as required by applicable federal regulations.  The JHSPH IRBs are authorized to conduct the review in accord with federal regulations using either (1) an expedited review process (see [Policy No. 110.1](https://www.hopkinsmedicine.org/institutional_review_board/guidelines_policies/organization_policies/110_1.html)) or (2) a convened review process (see [Policy No. 111.1](https://www.hopkinsmedicine.org/institutional_review_board/guidelines_policies/organization_policies/111_1.html)).  PIs are responsible for submitting continuing review applications containing sufficient information to allow the IRBs to determine whether the research may continue, should be modified, or should be terminated.

In determining how often continuing review should occur for studies under convened review, the JHSPH IRBs will consider the risks posed by the study intervention, what type of data and safety monitoring is provided for, and any other factors which affect the health and welfare of the study participants. IRBs may approve research for a defined time period of not more than one year minus one day, or for a limited number of subjects.  Once the period of approval is established, it will be communicated to the investigator in writing in the approval notification.

If protocol discrepancies or other concerns are identified during the continuing review process, the IRB may request verification of information from sources other than the investigators.  This step may be required if the IRB finds inconsistency with data submitted from previous years, determines there is a history of non-compliance with continuing review requirements, or believes unapproved changes have occurred since the last IRB approval of a protocol, or for any other cause.  The IRB may also request additional substantiation without cause.

The IRB has the authority to monitor the data produced by the study, the consent process, and the research itself through either the quality improvement specialist or independent consultants.

For protocols that require continuing review, approval automatically expires if a continuing review application is not submitted for IRB review prior to the expiration date.  In limited circumstances, the IRBs may permit continued study activity where the PI has submitted the continuing review application prior to the expiration date, but the IRB’s approval for continuation does not occur before that date (see [Policy No. 109.7)](http://www.hopkinsmedicine.org/institutional_review_board/guidelines_policies/organization_policies/109_7.html).

If the IRB determines that significant new findings regarding the research might affect participants’ willingness to continue taking part in the research, it has the authority to require provision of such information to participants.  This may include requiring re-consent of participants.

For studies where continuing review is not required by regulation the IRB may determine continuing review is required provided the rationale for this determination is documented as part of the IRB review process.

Additionally, as an alternative to continuing review, where continuing review is not required by regulation, the IRB has the authority to require that a progress report be submitted to the IRB. A progress report is an institutionally required study update that must be submitted to the IRB at a designated interval. The same report form will be used for Continuing Review and Progress Reports. The purpose of the progress report is to ensure the study is being conducted in a compliant manner and there are no issues with the conduct of the research that would prevent continued approval. Progress reports may be required at intervals of one, two or three years from the date of initial approval. The interval will be communicated in the approval notice.

## Policy No. 109.07 - Lapsed IRB Approvals

When the JHSPH IRB requires continuing review of previously approved human subjects research studies, it must occur on a timely basis.  Where continuing review is required, it is the PI’s responsibility to submit to the IRB a Continuing Review/Progress Report application on the timeline set by the IRB. Failure to timely submit will cause lapse of IRB approval, which is an incident of non-compliance.

OHRP and FDA place specific limitations on the conduct of research studies that have been submitted for IRB continuing review, but for which IRB approval lapses during the review process.  If a PI submits a Continuing Review/Progress Report application before the approval expiration, but the study approval lapses prior to IRB approval of that submission, no research activity may occur until the IRB approves the continuing review application. **New enrollment must stop when IRB approval lapses** in this circumstance.  The IRB, however, may take an action permitting continuation of study procedures with enrolled participants under certain limited circumstances as is consistent with federal guidance:

* OHRP’s “Guidance on Continuing Review” holds that study activity may continue for a brief time during this lapse in approval if it is in the “best interest” of the study participants.
* FDA’s “Guidance for Institutional Review Boards and Clinical Investigators” expresses the same basic concept where the investigator is actively pursuing renewal with the IRB and the IRB believes that an over-riding safety concern or ethical issue is involved.   In such cases the IRB may permit the study to continue for the brief time required to complete the review process.

The IRB will notify the PI if it determines that the study activity with enrolled participants may continue once approval has lapsed, including the length of time the activity may continue.  If IRB approval of a study will lapse after the continuing review/progress report application is submitted, but before the continuing review application will be discussed by the IRB, an IRB Chair may determine whether continued study activity will be permitted.  The PI will be notified of the IRB Chair’s decision.

**If a Continuing Review/Progress Report is not submitted to the JHSPH IRB prior to study lapse, the study will be terminated**.  No study activity, including non-interventional activity such as data analysis, may occur after the expiration date.  The JHSPH IRB does not have the authority to extend the approval period for a study, nor may it provide a “grace” period.  Submission of a new application may be required to obtain new JHSPH IRB approval.

## Policy No. 109.08 - IRB Monitoring of Ongoing Research

The JHSPH IRB has the authority to monitor ongoing IRB approved research at the institution. “Monitoring” includes auditing study documents, observing the consent process, and evaluating the implementation of all aspects of the IRB approved research plan. The IRB Director and Senior staff under the Institutional Official’s authority may observe consent processes, observe ongoing research procedures, interview research staff and participants, and evaluate study records as needed.

## Policy No. 110.01 - IRB Review of Research Using an Expedited Process

The JHSPH IRB may use an expedited review process to review new research applications in accord with DHHS and FDA regulations. Only research that (1) meets the regulatory definition of research involving “no more than minimal risk”, and (2) meets the criteria for one of the nine categories of research listed in the document “Categories Of Research That May Be Reviewed By The Institutional Review Board (IRB) Through An Expedited Review Procedure,” published by DHHS and FDA in the Federal Register, are eligible for an expedited review process. An expedited review process may be conducted for initial new applications, continuing review applications, or proposed minor changes in previously approved research.

An expedited review may be conducted by any member of the IRB whom the Chair determines has the required expertise, experience, and training. Reviews of research involving a drug, biologic, or CAM, must also be performed by the P&T member. The reviewer conducting the expedited review process has the authority to approve or table a study submission, but may not disapprove a submission. New applications, continuing review applications, or proposed changes in already approved research that a reviewer finds may not be approvable must be referred for discussion at an IRB meeting.

Research approved initially through a convened process may reach a stage at which it no longer requires continuing review: “Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study: (A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or (B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.” 45 CFR 46.109(f)(1)(iii).

The IRB may require a Progress Report to be reviewed via an expedited process.

Outcomes of expedited reviews will be made available to IRB members electronically so that they may review them and request that an expedited approval be put on a meeting agenda for re-review by the convened IRB.

## Policy No. 111.01 - Convened Meeting Primary Reviewer System

The JHSPH IRB will use a primary reviewer system to execute its convened meeting protocol review responsibilities for new review, continuing review, or amendment review. A primary reviewer will be identified for each study and will be assigned a specific application submission to prepare for presentation at the convened meeting.

The primary reviewer will consider the criteria for approval set forth in DHHS 45 CFR

46.111 and FDA 21 CFR 56.111, as applicable, in preparation for the presentation of the new application at the convened meeting. The IRB will consider the following as part of the initial review process:

• Purpose of the study and the value of the information sought

• Scientific validity of the study method and statistical plan

• Funding and qualifications of study personnel

• Subject selection: whether it is equitable, and appropriate to answer the study question

• Risk of harm to participants, and whether those risks are minimized

• Prospect of direct benefit to participants, and potential societal benefit of knowledge learned

• Risk/benefit ratio

• Recruiting plan including advertisements, telephone scripts

• Consent process – including training and experience of person obtaining consent; where, when, from whom consent will be obtained; assessment of understanding plus information given to participants as part of the consent process, including tools, (flip charts, etc.); evaluation of the informed consent document and the federally required elements of consent; whether consent will be documented, and if not, why not

• Vulnerable populations, and any additional protections they might require

• Privacy protections for study participant

• Data security issues, confidentiality of data, and what oversight authorities or Sponsors may see those data (FDA, IRB monitors, etc.)

• Data Safety Monitoring Plan (e.g., medical monitor, DSMB, etc.), if applicable.

• Study documentation, including information about investigational products (investigator brochures, drug data sheets, certificates of analysis, package inserts, diagrams or schematics for devices, Form 1572, etc.), study instruments (questionnaires, focus group guides, etc.)

* Data and biospecimen sharing, storage, and future uses

• If the new application research will take place internationally additional considerations are:

o How the PI will monitor the study, e.g. will the PI be on site, how often the PI will visit the site, how will communication with on-site researchers take place, etc.

o Local IRB approval

o Certificates of Translation of recruitment materials and consent forms

o PI management and oversight of the study

Documentation of convened review outcome will be recorded in the study minutes and

will be included in the JHSPH IRB study file. Documentation of Expedited Review will be recorded on the review form

## Policy No. 111.02 - Payment to Participants

The JHSPH allows payment to individuals who participate in research projects. The JHSPH IRB is authorized to review the amount and schedule of any proposed payment and to determine that it is fair and not an undue inducement to participate. Payment for participation in research should be reasonable and the amount paid should be comparable to other research projects involving similar time, effort, and inconvenience. For studies for which financial remuneration is a major reason for participation, and which represent minimum risk to the participants, the JHSPH IRB may approve remuneration that is sufficient to engage participants.

The IRB may approve research that includes a proposed bonus for completion and may determine that such payment would not unduly induce participants to stay in the study when they otherwise might have withdrawn. All information concerning payment, including the amount and schedule of payment(s), should be set forth in the informed consent document. Payment for participation in a trial offered by a sponsor may not include a coupon good for a discount on the purchase price of the product once it has been approved for marketing. Payment for participation may not include a discounted price for the provision of medical treatment.

## Policy No. 111.04 - Recruitment of Students and Employees

The JHSPH recognizes the ethical concerns that arise when Johns Hopkins students, postdoctoral fellows, or staff enroll as volunteers in Johns Hopkins research. These concerns relate primarily to the risks of possible undue pressure to enroll and potential loss of confidentiality. Targeted recruitment of students must conform to the Johns Hopkins University “[Policy Governing Recruitment and Enrollment of Students in Research](http://jhuresearch.jhu.edu/Policy_on_Student_Participation_in_Research_2.pdf) [Involving Human Subjects](http://jhuresearch.jhu.edu/Policy_on_Student_Participation_in_Research_2.pdf)”, and must be approved by the JHSPH IRB.

Targeted recruitment of employees, defined as employees of the University or Health System, must conform to the Johns Hopkins University “[Policy Governing Recruitment and Enrollment of Employees in Research Involving Human Subjects](http://jhuresearch.jhu.edu/Policy_on_Human_Subject_Recruitment%20-Employees_06.pdf)” and must be approved by the JHSPH IRB.

## Policy No. 111.05 - Scientific Review

The JHSPH requires compliance with [DHHS 45 CFR 46.111(a)(1)](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.111) and [FDA 21 CFR](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=56.111)

[56.111(a)(1)](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=56.111) regarding determinations that an IRB must make when non-exempt reviewing human subjects research. The JHSPH IRB is required to consider whether risks to participants are minimized, in part, by using procedures consistent with sound research design. The IRB review process will include an assessment of whether the research question asked in a proposed human subjects research project is valid and whether the study design appears to be appropriate. This regulatory requirement does not imply that the IRB will perform a level of review comparable to the NIH peer review process.

Many applications sent to the IRB have had prior scientific review by a qualified scientific body, such as NIH peer review. The JHSPH IRB may, but is not required to, consider such prior reviews to affirm in the review process that the research design is sound.

If outside scientific review has not been done and the reviewing IRB members have the expertise required to review a study, the IRB will be responsible for evaluating whether risks to subjects are minimized using sound scientific design. The reviewing IRB may use an outside consultant to supplement its review. The consultant shall be outside the IRB but may be within the Institution. Prospective consultants may not have any conflicts of interest, personal or financial, with the study, investigator, or sponsor. The consultant’s response will be available to the IRB during final deliberations on the study, and the IRB’s determinations will be documented in the minutes.

## Policy No. 111.07 - Sample Size

Principal Investigators must provide information regarding the number of participants to be enrolled in a research study. This number should be large enough to account for drop-outs, screen failures, or other complications that affect eligibility. Once accrual for the study reaches the number approved by the IRB, enrollment must cease. Enrollment of participants beyond the number of participants in the original, approved research plan may be considered non-compliance. For community-based studies that involve field workers enrolling large numbers of participants, it may be difficult to calibrate exactly how many individuals may agree to join a study. The IRB will use its judgement to determine whether over-enrollment for these studies represents non-compliance. The approved sample size is defined as the number of participants who sign the informed consent document, are enrolled using an oral consent process, or are “enrolled” with an IRB approved waiver of consent, as well as individuals who consent to being “screened” for eligibility.

While the anticipated sample size must be appropriate to answer the scientific question, failure to attain the original sample size does not constitute non-compliance. However, based on the magnitude of the under-enrollment, the IRB may ask for information on how this might affect the study’s ability to answer the research question.

An increase to the number of participants approved in the original research plan

requires an amendment to the IRB for review before enrolling the additional participants. The JHSPH IRB has the authority to modify the sample size. Enrollment may not continue above the original sample size until the IRB approves the amendment, which may be eligible for an expedited review.

## Policy No. 111.08 - Vulnerable Populations

Research conducted by JHSPH investigators often involves inclusion of populations that are referenced in federal regulations as “vulnerable populations.” The JHSPH IRB must evaluate the special considerations and protections that may be required to protect these populations. The specific populations mentioned in DHHS 45 CFR 46.111(a)(3) include “subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.” FDA 21 CFR 56 mentions “children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons.”

The JHSPH IRB will follow and document the application of specific DHHS and FDA subpart regulations pertaining to criteria required for IRB review and approval of research involving children, prisoners, and pregnant women/human fetuses/neonates.

For research involving participants who are vulnerable to coercion and undue influence and/or who are able to give consent, the IRB will permit their inclusion if the population is not specifically targeted as a matter of convenience, and the study recruitment and consent processes provide appropriate safeguards to protect the rights and welfare of these participants.

## Policy No. 111.09 - Investigators as Study Subjects

JHSPH faculty who wish to become involved as experimental participants in their own research projects should consider themselves to be “human participants.” The JHSPH IRB is authorized to review and approve faculty participation. Such review must occur before research procedures begin in an IRB approved study. There are two reasons for the required IRB review of proposed self-experimentation:

1) To protect faculty and staff from taking unwarranted risks in the excitement of generating new knowledge. Under these circumstances investigators are enthused about the prospect of new knowledge and concern for any associated risk may be minimized or escape attention; and

2) To protect the integrity of the research enterprise.

## Policy No. 111.10 - Assessing and Minimizing Risks in Human Subjects Research

All JHSPH research involving human subjects, exempt and non-exempt, should employ sound research principles and should minimize risks associated with participation. The IRB assesses the risk of harm posed to participants. Assessment of risk is based on comprehensive review of the potential physical, psychological, emotional, legal, social, and economic impact of the research on participants or the local community. The IRB must determine that the risk is reasonable in relation to anticipated benefits. If an intervention involves drugs, ingestibles (i.e., vitamins or food), or topical preparations, assessment of risk is further informed by examination of product information by the IRB P&T Committee liaison member, and presentation of that information to the IRB. The IRB will not approve research using these products without prior approval from the P&T member.

For studies that pose a higher risk of harm to participants that cannot be effectively minimized, the IRB annual continuing review of protocols may be adjusted to allow more frequent evaluation. The IRB may choose to impose either a) a more frequent review schedule (e.g., every 6 months) or b) a review schedule based on the number of enrolled participants (e.g., review after the initial 5 participants), or annually, whichever comes sooner. The IRB has discretion in implementing either strategy based on factors that include, but are not limited to, one or more of the following: nature and level of risks, particularly for intervention studies; experience of investigators overseeing study operation; or feasibility concerns, including recruitment, retention, and supervision. The review schedule will be communicated to the investigators at the time of initial approval and/or approval of a subsequent progress report. The review schedule may be modified upon demonstration of successful implementation of the study intervention or alleviation of any IRB concerns.

## Policy No. 111.11 - Conflict of Interest of IRB Members

JHSPH IRB members will not review, participate in the discussion of, or vote upon any research protocol for which they serve as principal investigator or co-investigator, or which is sponsored by a company in which the IRB member holds a financial interest, meaning anything of monetary value, including, but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g.,

stocks, stock options, or other ownership interests); and intellectual property rights (e.g., patents, copyrights, and royalties from such rights). Uncompensated relationships giving rise to a conflict of interest, such as board of directors or other executive service, would similarly disqualify a member. Additional conflicts may include:

• Involvement in the design, conduct, or reporting of the research;

• Involvement of immediate family members in the design, conduct, or reporting of the research; or

• Other involvement in the funding of the research, such as

o participating in the decision-making about providing grants or other awards to support the research, or

o serving as primary grantee for a training grant, program project grant, center grant or some other research funding and the successful completion of the activity under review could help demonstrate the success of the sponsored activity .

IRB members with these types of conflict of interest may provide information about the protocol, including reportable events of unanticipated problems or protocol non-compliance as requested by the IRB, then shall recuse themselves from the meeting during the discussion and vote on all such studies.

When a member, or a member’s spouse, relative or partner, is the PI on a study to be reviewed, the conflicted IRB member must leave the room for the IRB’s final discussion and vote.

## Policy No. 111.12 - Protecting Participant Privacy and Data Confidentiality

The JHSPH must review provisions for protecting the confidentiality of identifiable research data and patient health information as required for Exempt studies needing limited IRB review under 45 CFR 46.111(a)(7) and for all non-Exempt studies under the same provision. FDA regulated studies must meet the requirements of 21 CFR 56.111(a)(7). The JHSPH IRB sits as a HIPAA Privacy Board and must review all proposed disclosures of Protected Health Information for research purposes in accordance with its HIPAA policy. Confidentiality protections must meet state and local laws, and if the information or biospecimens are collected outside the United States, they must meet national requirements.

The IRB is authorized to ask the investigator to describe plans for protecting subject privacy and data confidentiality. If the study involves situations in which the participant has an expectation of personal privacy, the research plan should clarify how that privacy will be protected. The investigator’s plan must preserve the subject’s right to choose how and when his or her private information will be used, withheld, or disclosed. The consent process must disclose to participants the potential risks of a breach of the subject’s right to privacy and data confidentiality. The IRB may determine additional methods as needed to minimize the risk.

All federally funded research protected by a Certificate of Confidentiality should include a description of that protection in the consent documents. The PI also must clarify in the consent document that the PI voluntarily will report any reportable information disclosed by a participant about child abuse or neglect, or threats of harm to self or others.

## Policy No. 111.13 - Recruiting Study Subjects

The JHSPH IRB will review recruitment plans for research projects to evaluate participant selection. To that end, the research application must provide the characteristics of the participant population and criteria for inclusion or exclusion. The JHSPH IRB is authorized to review the purposes of the research, the setting of the research, and whether the population to be recruited is appropriate to achieve those purposes under the specified plan. The IRB will evaluate whether the proposed population is vulnerable and requires special protections. Regulatory determinations will be made if a project proposes to recruit pregnant women (45 CFR

46 Subpart B), prisoners (45 CFR 46 Subpart C), or children (45 CFR 46 Subpart D, and 21 CFR 50 Subpart D).

The JHSPH IRB will assess the recruitment plan to ensure that it is compliant with federal regulations as well as HIPAA Privacy Policies, and the institutional policies governing recruitment of students and employees (JHSPH Policy 111.04).

All letters to potential participants and locally posted flyers or other recruitment material must be reviewed and approved by the IRB prior to use.

When direct advertising is to be used, the IRB must review and approve the information contained in the advertisement and the mode of its communication. This includes the final copy of language and images to be used in printed advertisements, web postings and websites. The IRB must approve language in a recorded (video, audio) advertisement prior to recording, and all social media and related messaging.

## Policy No. 112.01 - Review and Disapproval of IRB Approved Research by Institution Officials

Review of IRB approved research may be conducted by senior Institutional officials:

* IO (Vice Dean for Research),
* Dean of the JHSPH
* Deans of the JHU Schools at which the approved research is to be conducted, President of JHHS, and/or the President of the respective JHHS hospital at which the research is to be conducted
* General Counsels of JHU or JHHS (when research is conducted at a JHHS facility).

These officials are authorized to disapprove JHSPH IRB approved research projects in extraordinary circumstances if they may pose harm to the Institution.

Such actions will be communicated to the PI, with an explanation of the rationale for disapproval. Communications of institutional disapproval may be provided to the PI in writing or by e-mail communication.

An action taken by an institutional official to disapprove an IRB approved project is final and no further appeal is possible. The PI of a disapproved research project may submit a new application to the JHSPH IRB that includes modifications to address the reason for Institutional disapproval. Institutional officials may not approve research that has been disapproved by the IRB.

## Policy No. 113.01 - Suspension or Termination of IRB Approved Research

The JHSPH IRB may suspend or terminate active human subjects research projects. The IRB may determine that a project should be suspended or terminated due to number of factors, including unanticipated problems involving risk to subjects or others under Policy 103.06, serious or continuing non-compliance under Policy 103.07, findings presented in the continuing review process or amendment review process (e.g., new scientific information or a DSMB report), or problems identified in a monitoring process.

The IO and IRB Chairs have the authority to suspend or terminate human subjects research when an event occurs without waiting for a convened IRB review if they determine it is necessary to act to protect the rights and welfare of participants. An action taken by the IO or an IRB chair to suspend or terminate research will be reported to the reviewing IRB at the next convened meeting.

“Suspension” of research is defined as a temporary or permanent halt to some or all research procedures, short of a termination, until the IRB determines whether the research may recommence (with or without modifications to the research) or whether the research must be terminated.

“Termination” of research means a permanent stop to the research and all research- related activities. In the context of this policy, “termination” means an early stop to the research, short of the “natural” end of the study, for cause.

Suspension or termination of approval shall be documented in a written notice to the PI. The notice of suspension or termination of IRB approved research must include a statement of the reasons for the action. The communication to the PI will offer to the PI an opportunity to respond to the decision. The communication will ask the PI to provide a plan for ensuring that the rights and welfare of all currently enrolled, or previously enrolled (if appropriate), participants are protected.

The IRB will determine and inform the PI of steps to be taken as a result of suspension or termination of the research. Steps could include:

* Withdrawal of participants, considering the rights and welfare of those individuals before such a step is taken;
* Notification of currently enrolled participants that the study has been terminated by a written communication approved by the IRB. In this case, communication to participants will explain the rationale for the action taken;
* Informing the participants of any follow-up procedures permitted or required by the IRB for participant safety; and
* Submission of reports to the IRB and the sponsor of any adverse events/outcomes that occurred during period when suspension or termination occurred.

The IRB must report in writing the suspension or termination to the IO. Reports to the IO must be sent within 30 days of the IRB’s determination to suspend or terminate, or sooner in cases where the rights and welfare of enrolled participants requires immediate attention by the IO and the Institution. The IO will follow JHSPH policy regarding reporting the suspension or termination of a study to federal agencies.

## Policy No. 114.02 – Reliance Agreements, Cooperative Research and Multi-Center Studies

As part of its responsibility for safeguarding the rights and welfare of human participants in research, the JHSPH IRB has the option of entering into reliance agreements with other institutions. The JHSPH may rely upon the review of an external IRB, or may assume responsibility for IRB oversight on behalf of another institution. The JHSPH IRB will not serve as a Single IRB under 45 CFR 46.114(b); JHSPH investigators with grants requiring JHU to serve as a Single IRB may submit their research applications to the JHU School of Medicine IRB. JHSPH investigators involved in Single IRB studies may submit a Reliance Request application asking the JHSPH IRB to rely on an external Single IRB. These reliance agreements are options for non-exempt studies and for exempt studies that require limited IRB review under 46.104. JHSPH and the external institution will document their agreement and will clarify the responsibilities that each entity will undertake to ensure compliance with the federal, state, and local regulatory requirements, and with institutional policies.

## Policy No. 115.01 - IRB Record Keeping

The JHSPH IRB Office shall maintain documentation of all IRB activities in accordance with federal regulations 45 CFR 46.115 and 21 CFR 56.115. The IRB Office shall keep the following records:

1. Copies of all research applications, research plans (and when applicable, federal funding applications)   
reviewed; and all material and documents submitted with the proposals for IRB review, including:

* Approved sample consent documents
* Continuing Review/Progress reports
* Amendments to approved research
* Reports of injuries, complaints, and other events (whether anticipated or unanticipated)
* Final study reports

2. Minutes of IRB meetings that document discussions and decisions about research under review. A minutes template shall be used to document:

* Attendance at the meeting for each vote
* Conflict of interest determinations
* Device risk determinations
* Drug issues
* Regulatory risk determinations for children, pregnant women/fetuses, and prisoners, or other identified vulnerable populations
* Justification for waiver or alteration of informed consent or documentation of informed consent
* The basis for requiring changes to proposed research, tabling decisions, or disapproval of research
* Discussion of controverted issues and their resolution
* Actions taken by the IRB
* The vote on these actions including the number of members voting for, against, and abstaining

3. Copies of all correspondence between the IRB and investigators, DSMB, and other entities involved in the research or institutional officials (as applicable)

4. A list of all IRB members, both primary members and alternates. The list shall identify the member’s name, earned degrees, member category (non-scientist, physician scientist, or other scientist) research experience, experience and expertise applicable to IRB deliberations. For non-JHSPH affiliated members, affiliation status and whether the member or an immediate family member is affiliated with a division within the Johns Hopkins University or medical institutions.

5. Written JHSPH IRB policies and operations procedures.

6. Statements of significant new findings required to be provided to research participants as required by regulations.

All JHSPH IRB records associated with specific research proposals are retained indefinitely. An off-site storage facility shall be used to store archived hard copy materials; other records may be stored in secure electronic systems. All records shall be accessible and available for inspection by authorized agency personnel at reasonable times and in a reasonable manner.

## Policy No. 115.02 - Record Retention Requirements for Investigators

All principal investigators must maintain copies of all research documents in accordance with federal requirements and institutional policies in a protected, secure manner. In general, although there are exceptions, under institutional policy faculty members are required to maintain research records for 5 years.

The following is a list of commonly encountered additional regulatory requirements governing the length of time records must be retained:

Federal Regulations

HIPAA: Since HIPAA entitles participants to an accounting of all uses and disclosures of Protected Health Information (PHI) for six years after their participation in a study is completed, records for all studies that involve PHI from a Johns Hopkins covered entity should be retained for at least seven years; for minors, that’s seven years after they reach the age of majority. For PHI received from other covered entities, investigators should check their agreement with the covered entity for any tracking and data retention requirements.

FDA - Investigational New Drug (IND) Applications: Research records for studies that involve INDs must be retained by the investigator during the study and “for a period of 2 years following the date a marketing application is approved for the drug for the indication of which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.” (21 CFR 312.57)

FDA - Investigational Device Exemptions (IDE): Research records for studies that involve IDEs must be retained by the investigator during the study and “for two years after the latter of the following two dates: the date on which the investigation is terminated or completed, or the date that the records are no longer required for supporting a premarket approval application or a notice of completion of a product development protocol.” (21 CFR 812.140(d)).

## Policy No. 116.01 - Informed Consent Process

The JHSPH IRB will review the proposed consent process associated with all studies that involve an interaction or intervention with a human subject. Investigators must seek legally effective informed consent under circumstances that provide the prospective participant with sufficient time and opportunity to consider whether or not to participate, and that minimize the possibility of coercion or undue influence. The information must be presented in language understandable to the participant and must include information that a reasonable person would want to know in order to make an informed decision with an opportunity to ask questions.

The IRB’s evaluation of the investigator’s proposed participant selection/recruitment process and informed consent process will include:

* How the PI plans to identify potentially eligible participants;
* How the PI plans to approach potentially eligible participants;
* What the PI plans to communicate to potential participants to see if they are interested in learning more about the study;
* Review of all recruitment and consent materials, including flyers, social media language, advertising, etc.;
* Determining whether the consent materials include all the elements of informed consent appropriate for the particular study;
* If minors are involved, who has the legal authority to provide consent for them to join the study (parent, legal guardian, or the minors themselves);
* If minors are involved, and assent is required, what kind of assent materials are appropriate for them;
* Consideration of the capacity of the participant to make an independent and voluntary informed decision whether or not to participate in a study, and if they lack capacity, who has legal authority to provide informed consent;
* Review of who will obtain consent, that person’s qualifications and human subjects research and compliance training, and under what circumstances consent will be obtained;
* Determination of how the investigator will assess the understanding of the participant, if appropriate; and
* Deciding whether consent will be documented.

The information to be presented to a potential participant, in a written or oral form, and as a whole must present information in sufficient detail that facilitates the participant’s understanding of the reasons that they may or may not want to participate in the study. The informed consent may not include any language which waives, or appears to waive, any of the participant’s legal rights, or releases or appears to release the parties to the research from liability for negligence.

## Policy No. 116.02 - Informed Consent Documentation

JHSPH investigators may enroll participants in human subjects research activities only after the IRB has approved the study, and when required by the IRB, the investigator obtains the participant’s legally effective informed consent. The JHSPH will review both the proposed informed consent process, and the documentation associated with that process.

JHSPH investigators must comply with the informed consent requirements of 45 CFR

46.116 (for DHHS regulated studies) and 21 CFR 50.20 (for FDA regulated studies). Documentation of informed consent will be required, with all the required elements of informed consent and all appropriate additional elements, unless the research activity meets the criteria for waiver or alteration of the elements of informed consent. For these studies, the IRB may waive consent entirely or may waive certain of the

required elements of consent from the consent document, depending upon what may be required to obtain “legally effective” informed consent from the study population. The IRB may also waive documentation of informed consent under 45 CFR 46.117(c), or 21

CFR 56.109(c) for FDA regulated studies, and permit an oral consent process in appropriate cases.

The JHSPH IRB will post Consent Form Templates with all the required elements of informed consent and will post guidance for investigators explain what is required for research applications. The consent forms used to enroll participants must be marked with a current IRB stamp or logo, unless waived by the IRB.

## Policy No. 116.04 - Informed Consent from non-English Speakers

Federal regulations require that consent be obtained in a language understandable to the subject. The consent process, and documentation (if applicable), must satisfy this requirement.

For studies that may involve non-English speakers, the IRB may approve either a translation of the English version, with a Certificate of Translation signed by the PI, or a short form translated into the participant’s language explaining that the required elements of informed consent, including key information, will be provided to the potential participant. The consent process using the short form will include a translation of the full consent document in the potential participant’s language, and a witness to that oral discussion who will sign the short form along with the potential participant.

For some international studies, study participants may speak a language that is not written, thus making documentation impossible. In such cases, the study must provide a consent process that ensures that information is provided orally in that unwritten language.

## Policy No. 116.05 - Use of Research Data in Cases of Questionable Consent Documentation

Research projects that are conducted over time may experience problems with study documentation. Changes in study personnel, including change in the PI, may result in confusion about where original consent forms are filed or stored. The JHSPH IRB periodically receives requests from PIs to use data in cases where consent documentation is in question. The JHSPH IRB may consider use of data in

these cases only as follows:

When data continues to be collected through interaction with participants or the PI has knowledge that the subject population is still available for contact, the PI may be able to re-consent the participants before continuing to use the existing data or collect additional data. Data from any individuals who do not re-consent when approached must be discarded. Contact with participants to ask for re-consent must be through use of an IRB approved document.

When data exist and interaction with participants is not possible (either due to relocation of the participants, participant is lost to follow-up, or is deceased), data may be used only if the research record (or the medical record) contains a note that a research consent was obtained and in the case of biospecimens, the IRB approved consent form did not contain an opt out provision for subjects to indicate they did not wish their samples to be used for research purposes. The note in the record must specify who obtained the research consent and the date on which it was obtained. If a note exists in the record, but the consent form approved by the IRB contains an opt-out provision, the data must be discarded, as one could not determine that a subject had or had not restricted future use of their data. If the research record or medical record does not contain a note attesting to consent having been obtained, data must be discarded.

Samples and data from pediatric populations represent a unique case. If the consent form is not available to indicate parental permission was granted, in writing, to obtain a sample/data for research purposes, data/specimens may not be used in the research.

## Policy No. 117.01 - Signing the Consent/Assent Document

The JHSPH requires that participants must sign and date a research consent form before study intervention or procedures begin unless the reviewing IRB approves and documents exceptions meeting federal regulations. The person obtaining informed consent must sign and date the form at the time and on the date that the participant signs it, unless the consent process approved by the IRB indicates otherwise. The JHSPH IRB does not require a witness signature line, but may allow use of consent forms that have a witness signature line.

For research involving pediatric participants, the IRB must determine whether to require an assent form or an assent statement within the parent/guardian consent document. If the IRB determines that a child is old enough and mature enough to sign the consent form as documentation of assent, an assent signature line must be provided. For research approved under 45 CFR 46.406, 21 CFR 50.53, 45 CFR 46.407, and 21 CFR 50.54, both parents (when applicable according to the regulations) must sign and date the consent form, and the consent form must have signature lines for each parent. For research approved under 45 CFR 46.404, 21 CFR 50.51, 45 CFR 46.405 or 21 CFR 50.53, the IRB will determine whether the signature of both parents is required or whether the signature of one parent is sufficient. The proper number of signature lines must be provided in accordance with IRB review and approval.

For research involving adults lacking capacity to consent for themselves, the consent form must provide a signature line for the legally authorized representative who will sign and date the consent form on behalf of the adult subject.

## Policy No. B203 - Research Involving Pregnant Women, Human Fetuses, and/or Neonates as Participants

The JHSPH will adhere to DHHS regulations regarding additional protections required for non-exempt research involving pregnant women, fetuses, and neonates. In addition to the other responsibilities assigned to the JHSPH IRB under 45 CFR Part 46 Subpart A, the IRB will determine whether pregnant women may or may not be included in research (45 CFR 46 Subpart B, 46.203), and if so, whether all appropriate safeguards are in place. The required regulatory findings must be documented when the IRB knows that pregnant women or neonates may be included in the research population, the research requires convened review, and the IRB determines that the research procedures are more than minimal risk. The IRB will not make the regulatory findings for minimal risk studies that qualify for review by an expedited process except for

studies that specifically target pregnant women. For research that will involve neonates, the IRB must make required regulatory findings and document the determinations.

## Policy No. C304 - Research Involving Prisoners as Participants

For the purposes of human subjects research, a prisoner is defined in 45 CFR 46.303(c) as “any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.”

JHSPH is "engaged" in research involving prisoners when both of the following circumstances apply:

1. The investigator obtains data through intervention or interaction with a prisoner, or identifiable private information about a prisoner; AND
2. The investigator knows that one or more of the data subjects includes a person whose circumstances meet the regulatory definition of "prisoner" under 45 CFR 46.303(c).

For the research to "involve" prisoners, the investigator must have actual knowledge of circumstances that would cause a subject to fall under the regulatory definition. Investigators do not need to determine prospectively whether each potential subject is or may become a prisoner.

Prisoners may not participate in exempt research unless the research aims at involving a broader participant population that only incidentally includes prisoners.

For all non-exempt research involving prisoners requiring convened review, an IRB member who qualifies as a prisoner representative must be present at the convened meeting of the IRB and during the presentation, discussion, and vote of any study which involves prisoners. A majority of the IRB members (exclusive of prisoner members) must have no association with the prison involved, apart from their membership on the IRBs.

The prisoner representative:

* Must be a voting member of the IRB.   This individual may be listed as an alternative member who becomes a voting member when needed.
* Must review research involving prisoners, focusing on the requirements in Subpart C or equivalent protections. The prisoner representative must receive all review materials pertaining to the research that are received by the primary reviewer.
* Must be present at a convened meeting when the research involving prisoners is reviewed. If the prisoner representative is not present, research involving prisoners cannot be reviewed or approved.  Attendance may be by phone, video-conference, or webinar, as long as the representative is able to participate in the meeting as if they were present in person at the meeting.
* Must present his/her review either orally or in writing at the convened meeting of the IRB when the research involving prisoners is reviewed.

The JHSPH IRB must make the required determinations when reviewing an application involving prisoner research.

Continuing review and review of more than minor changes to the research must occur using the same procedures for initial review, including the responsibility of the prisoner representative to review the continuing review materials and participate in the meeting (as described above).  If no participants have been enrolled, the research may receive continuing review using the expedited procedure under expedited category #8.

Minor modifications to research involving prisoners may be reviewed using the expedited procedures.

For studies originally reviewed and approved by the IRB without prisoners as participants, if the PI learns that a participant has become a prisoner during the study, the PI must submit a Problem Event Report to inform the JHSPH IRB of the individual’s change in status.  In this report, the PI must indicate whether the individual’s incarceration is expected to be temporary and, if not, whether the PI intends for the subjects to continue as a participant while incarcerated.  If so, the PI must also submit an Amendment, requesting IRB approval for prisoners as a study population under Subpart C. The JHSPH IRB must make the final determination whether the subject may continue as a participant.

Prisoners may not be included in Department of Defense-regulated research.

## Policy No. D403 - Research Involving Children as Participants

The JHSPH IRB will follow federal regulations regarding the additional responsibilities assigned to the IRB under DHHS regulations [(45 CFR 46 Subpart D)](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#subpartd) and FDA regulations ([21 CFR 50 Subpart D](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50&amp;showFR=1)), as applicable. These regulations provide additional protections for children who participate in research. For the purpose of applying Subpart D of the federal regulations, children are defined as persons who have not attained the legal age for consent to treatments or procedures involved in the research, and who do not fall within any of the legal exceptions under the applicable law of the jurisdiction in which the research will be conducted.

The JHSPH IRB must review all non-exempt research covered by Subpart D, and will approve only research that satisfies the conditions of all applicable sections of Subpart D. The IRB must determine that whenever Subpart D applies, consent will be obtained in accordance to the requirements of Subpart D; e.g., from each child subject’s parents or guardians as required, in addition to the child’s assent (when applicable). These findings will be documented.

Under DHHS regulations, “guardian” means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care; and under FDA regulations “guardian” means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care

when general medical care includes participation in research. For purposes of subpart D of this part, a guardian also means an individual who is authorized by law to consent on behalf of a child to participate in research.

The JHSPH IRB may approve research applications include children in foster care, so long as all federal, state, and local requirements are met.

Under Maryland law, individuals younger than 18 years of age are considered “children” as defined in Federal regulations, unless a statutory exception broadens the definition.

Requirements for Assent by Children

“Assent” means agreement – specifically, in this context, a child’s agreement to participate in research. Assent, like consent, is a process that must be documented.

Under [45 CFR 46.408(a),](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.408) if the IRB determines that children are capable of providing assent, the IRB must determine that adequate provisions are made for soliciting their assent. The IRB will additionally consider how assent will be solicited, obtained and documented. In determining whether children are capable of assenting, the IRB takes into account their ages, maturity, and psychological state. This judgment may be made for all children to be involved in research under a particular protocol, or for each child,

as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, then the IRB may determine assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the participants are capable of assenting, the IRB still may waive the assent

requirement in accord with [45 CFR 46.116](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.116).

Documentation of Assent

Under [45 CFR 46.408(e),](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.408) when the IRB determines that assent is required, it shall also determine whether and how assent must be documented. The assent should be written at the age level of the children, with jargon and technical terms explained or removed.

For children aged approximately seven and under, the IRB may determine written documentation is not required, but that Investigators must verbally explain the study to the child, including its purpose, procedures, and potential risks and benefits (if appropriate, depending on the child’s age, maturity and development). For children ages eight through 17 years, the IRB may require separate written assent from the child, or may allow an affirmative statement in the parental permission form to provide documentation of assent.

Depending on the study, its procedures, risk and benefits, the IRB may approve an oral assent process with written documentation made in the record that an assent discussion occurred.

## Policy No. FDA 312/812 - Clinical Investigations with FDA Test Articles

The JHSPH IRB has the authority to review and approve studies involving FDA regulated “test articles.” Test articles may include drugs, botanicals, biologics, gene therapy, and medical devices, as defined under FDA regulations on protection of human subjects ([21 CFR 50](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50) and [21 CFR 56](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56)), and the Investigational New Drug (IND) and Investigational Device Exemption (IDE) regulations ([21 CFR 312](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRsearch.cfm?CFRPart=312) and [21 CFR 812](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=812)).

## Policy No. FDA 50.1 - In Vitro Diagnostic Device Research

In Vitro Diagnostics (IVDs) are reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, to cure, mitigate, treat, or prevent disease. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body.

IVDs that are being tested for possible future marketing are devices, and may also be biological products. They are test articles under Food and Drug Administration regulations and are subject to FDA regulations governing investigational devices (IDE regulations). When IVDs are used in research involving human subjects (or human samples), FDA’s regulations for the protection of human subjects (informed consent and IRB review) generally also apply.

IDE Exempt Studies

Studies may be exempt from FDA’s IDE regulations when the research meets all of the following criteria:

* The sponsor has labeled the device properly;
* The testing is non-invasive;
* The testing does not require an invasive sampling procedure that presents significant risk;
* The testing does not by design or intention introduce energy into a participant; and
* The testing is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically-established diagnostic product or procedure.

Investigators should also be aware that IVD testing performed in the laboratory setting is subject to the requirements of the Clinical Laboratories Improvement Act (“CLIA”). If an investigator intends to share results of an IVD test with research subjects or their care providers, the IRB must be informed of this fact.

IRB Review

Unlike DHHS regulations, FDA regulations do not provide for exemption from IRB review when research involves existing specimens and the investigator records information without identifiers or linking codes. Nor do FDA regulations define “human subjects” with reference to the identifiability of the subject or of the subject’s private information (i.e., the donors of specimens/samples remain “human subjects” even when the specimens/samples are de-identified). Current FDA guidance indicates that IRB review is required for any IVD study involving human specimens/samples, even when the research involves no identifiers and the biological materials cannot be linked to any identifying information.

Informed Consent

With a few narrow exceptions (i.e., emergency and some DOD research), FDA regulations do not permit waiver of consent, even when studies are minimal risk and would meet criteria for waiver of consent under DHHS regulations. Under FDA regulations, informed consent is required for IVD studies involving samples that are identifiable (i.e., are labeled with identifiers or accompanied by the patient’s identifiable clinical information), as well as for studies in which the samples are not identifiable but are coded or linked to identifiable information.

Current FDA guidance (4/25/06), however, indicates that under some circumstances, when samples taken from excess clinical or research specimens cannot be identified (e.g., all linking codes and identifiers have been removed, or the investigator has no access to the code keys or identifying information), the agency will exercise “enforcement discretion” and permit the IRB to approve the study without requiring informed consent of the sample sources.

To be eligible for approval without a requirement for informed consent, FDA indicates that IVD research must meet the following criteria:

* The research must be conducted under an IRB-approved protocol;
* The research must meet criteria for an IDE exemption;
* The research must use specimens left over from clinical care, specimen repositories, or other research (i.e., the specimens may not be collected specifically for the proposed research, and no additional specimen may be collected for the purpose of research);
* Individuals caring for the patients are different from and do not share information about the patient with those conducting the investigation[\*](http://irb.jhmi.edu/Policies/FDA50_1.html#asterick%23asterick);
* The specimens are provided for research without identifiers (codes are permissible only if neither the investigator nor anyone associated with the study has access to the code key or can identify the person who was the source of the specimen);
* Any clinical information supplied with the specimen must not be individually identifiable. No test results from the research may be reported to any subject or that subject’s health care provider; and
* The supplier of the specimens must have established policies and procedures to prevent the release of identifying information.

## Policy No. SL1 - Adherence to the Hubbard Act

Johns Hopkins complies with Maryland law concerning human subjects research and IRB approval of such research.  Pursuant to the Maryland Annotated Code, Health-General Article §13-2003 (The Hubbard Act), any person who wishes to inspect the final minutes from a JHSPH IRB convened meeting held after October 1, 2002 may do so by submitting a written request outlining the specific minutes to be inspected.  The interpretation by JHU General Counsel is that the law is prospective in application and does not apply retrospectively to IRB minutes that existed prior to October 1, 2002.  Prior to making the minutes available, the IRBs may redact confidential or privileged information.

A written request under this law should be submitted to the JHSPH IRB Office.

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## Policy No. SL2 - State of Maryland Mandatory Reporting Requirements

JHSPH investigators who collect information about reportable diseases, or who may learn about abuse or neglect of a child or vulnerable adult, must address in their research applications and consent documents their obligation to report to legal authorities. The JHSPH IRB may require disclosure in the consent form of other reports that an investigator may voluntarily choose to make.

**I. Reportable Diseases and Conditions**

JHU must comply with the State of Maryland mandatory reporting regulations.  The list of reportable diseases and conditions is updated periodically and may be found at the Maryland Department of Health web site (<https://phpa.health.maryland.gov/Pages/reportable-diseases.aspx>.)

The JHSPH IRB and its PIs must adhere to the requirements associated with Certificates of Confidentiality, when applicable. Information is available at <http://grants1.nih.gov/grants/policy/coc/cd_policy.htm>for options for addressing local reporting requirements in studies for which a Certificate of Confidentiality is granted.

**II. Child or Elder Abuse or Neglect**

Under Maryland law, any person, whether or not a “health care provider”, is required to report suspected child abuse or neglect. Health care providers must make these reports in specific oral and written forms. Although licensed providers are obligated to

report suspected neglect or abuse of a vulnerable adult, non-provider investigators, who are permitted but not obligated to make such reports for adults, may be precluded from doing so if the reporting involves disclosure of protected health information. However, HIPAA may restrict disclosure of PHI to reports of adult abuse or neglect to those circumstances under which the report is required by law or the circumstances constitute an emergency.

**III. Threats of Harm**

Investigators who are mental health providers licensed under the Health Occupations Article have a statutory duty to warn of a patient’s threats to inflict imminent physical harm upon specific victims. This duty may be discharged by “reasonable and timely” efforts to inform law enforcement and the identified victims. The statutory language implies but does not specifically require a patient-provider relationship, so it is possible that the duty to warn might be found to extend to certain research settings involving investigators who are mental health providers.