

Human Research Protection Program

Standard Operating Procedures

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Division of Academic Affairs

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1 Human Research Protection Program

Baystate Health. and its affiliates (hereafter, *BH, Baystate or the Institution*) fosters a research environment that promotes the respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of the institution. Baystate is comprised of all locations of Baystate Medical Center, Baystate Franklin Medical Center and Baystate Mary Lane Hospital and any other affiliate of Baystate Health where research may be conducted.

In the review and conduct of research, actions by Baystate are guided by the principles (i.e., respect for persons, beneficence, and justice) set forth in the ***Ethical Principles and Guidelines for the Protection of Human Subjects of Research*** (often referred to as the [Belmont Report](#)). The actions of Baystate also conform to all applicable federal, state, and local laws and regulations. In order to fulfill this policy, Baystate has established a Human Research Protections Program (HRPP).

1.1 Mission

The mission of the HRPP is to:

- Safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are protected;
- Provide timely and high quality education, review, and monitoring of human research projects.
- Facilitate significant and innovative research involving human subjects;
- Facilitate excellence in the conduct of research involving human subjects;

The HRPP includes mechanisms to:

- Establish formal processes to monitor, evaluate, and continually improve the protection of human research participants.
- Dedicate resources sufficient to do so.
- Exercise oversight of research protection.
- Educate investigators and research staff about their ethical responsibilities to protect research participants.
- Proactively identify and respond directly to concerns of research participants.
- When appropriate, intervene in the conduct of research.

1.2 Institutional Authority

The Baystate Human Research Protection Program (HRPP) was established by an authorizing vote of the institution's Board of Trustees on 10/14/2009. As stated in that vote, the operating procedures in this document "...serve as the governing procedures for the conduct and review of all human research conducted under the auspices of Baystate Health". A copy of the authorizing vote and these operating procedures are made available to all Baystate investigators and research staff. Additionally these operating procedures are posted on the Baystate intranet.

1.3 Definitions

Common Rule The Common Rule refers to the "Federal Policy for the Protection of Human Subjects" adopted by several federal agencies. Although the Common Rule is codified by each agency separately, the text is identical to DHHS regulations in 45 CFR 46 Subpart A. For the purposes of this document, references to the Common Rule cite the DHHS regulations.

Human Subjects Research – means any activity that meets the definition of "research" and involves "human subjects" as defined by either the Common Rule or Food and Drug Administration (FDA) regulations.

Research The Common Rule defines research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge.

For the purposes of this policy, a "**systematic investigation**" is an activity that involves a prospective study plan that incorporates data collection, either quantitative or qualitative, and data analysis to answer a study question. Investigations designed to develop or contribute to **generalizable knowledge** are those designed to draw general conclusions (i.e., knowledge gained from a study may be applied to populations outside of the specific study population), inform policy, or generalize findings.

Research as defined by FDA regulations means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be later submitted 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 synonymous for purposes of FDA regulations. [21 CFR 50.3(c), 21 CFR 56.102(c)]

Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act" means any

use of a drug other than the use of an approved drug in the course of medical practice. [21 CFR 312.3(b)]

Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act” means any activity that evaluates the safety or effectiveness of a device. [21 CFR 812.2(a)]

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

Human Subject A human subject as defined by the Common Rule is a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or through identifiable private information (45 CFR 46.102(f)).

- Intervention means both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes.
- Interaction means communication or interpersonal contact between investigator and subject.
- Private information means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).
- Individually identifiable information is information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

For research covered by FDA regulations (21 CFR 50 and 56), human subject means an individual who is or becomes a participant in a clinical investigation, either as a recipient of the test article or as a control. A subject may be in normal health or may have a medical condition or disease. In the case of a medical device, a human subject/participant also includes any individual on whose tissue specimen an investigational device is used or tested.

Note: The terms “subject” and “participant” are used interchangeably in this document and have the same definition.

Test Article. A test article is a drug, device, or other article including a biological product that is the object of a clinical investigation involving human subjects or their specimens. Test articles covered under the FDA regulations include:

- a. **Human drugs** – The primary intended use of the product is achieved through chemical action or by being metabolized by the body. A drug is defined as a substance recognized by an official pharmacopoeia or formulary: A substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; A substance (other than food) intended to affect the structure or any function of the body; A substance intended for use as a component of a medicine but not a device or a component, part or accessory of a device.
<http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm>
- b. **Medical Devices** - A device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them; intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of it's primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."
<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051512.htm>
- c. **Biological Products** - include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources — human, animal, or microorganism — and may be produced by biotechnology methods and other cutting-edge technologies. Gene-based and cellular biologics, for example, often are at the forefront of biomedical research, and may be used to treat a variety of medical conditions for which no other treatments are available.
<http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm>
- d. **Food Additives** - In its broadest sense, a food additive is any substance added to food. Legally, the term refers to "any substance the intended use of which results or may reasonably be expected to result -- directly or indirectly -- in its becoming a component or otherwise affecting the characteristics of any food." This definition includes any substance used in the production, processing, treatment, packaging, transportation or storage of food.
- e. **Color Additives** - A color additive is any dye, pigment or substance which when added or applied to a food, drug or cosmetic, or to the human body, is capable (alone or through reactions with other substances) of imparting color.
<http://www.fda.gov/Food/FoodIngredientsPackaging/ucm094211.htm#foodadd>
- f. **Foods** - Foods include dietary supplements that bear a nutrient content claim or a health claim

- g. **Infant Formulas** – Infant formulas are liquid foods intended for infants which substitute for mother’s milk

Institutional Review Board (IRB). An IRB is a board designated by the Institution to review, to approve the initiation of, and to conduct periodic review of research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The IRB may be assigned other review functions as deemed appropriate by the Institution.

Institutional Official (IO) The IO is responsible for ensuring that the HRPP has the resources and support necessary to comply with all federal regulations and guidelines that govern human subjects research. The IO is legally authorized to represent the institution, is the signatory official for all Assurances, and assumes the obligations of the institution’s Assurance.

Research Under the Auspices of the Institution Research under the auspices of the institution includes research conducted at BH, conducted by or under the direction of any employee or agent of BH (including students) in connection with his or her institutional responsibilities, conducted by or under the direction of any employee or agent of BH using any property or facility of BH, conducted by or under the direction of any individual or entity using any property or facility of BH, or involving the use of BH’s non-public information.

Engagement in Research Institutions are considered [engaged](#) in a research project when the involvement of their employees or agents in that project includes any of the following:

- Intervention for research purposes with any human subjects of the research by performing invasive or noninvasive procedures.
- Intervention for research purposes with any human subject of the research by manipulating the environment.
- Interaction for research purposes with any human subject of the research.
- Obtaining the informed consent of human subjects for the research.
- Obtaining for research purposes identifiable private information or identifiable biological specimens from any source for the research. In general, obtaining identifiable private information or identifiable specimens includes, but is not limited to:
 - observing or recording private behavior;
 - using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided by another institution; and

- Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the investigators.

Institutions are not considered to be engaged in human subject research if its employees or agents perform commercial or other services for the researcher at the institution, provided that all of the following conditions also are met:

- the services performed do not merit professional recognition or publication privileges;
- the services performed are typically performed by those institutions for non-research purposes; and
- The institution's employees or agents do not administer any study intervention being tested or evaluated under the protocol.

Agent Agents include all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility.

1.4 Ethical Principles

Baystate is committed to conducting research with the highest regard for the welfare of human subjects. It upholds and adheres to the principles of *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects in Research* by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1979). These principles are:

- 1) **Respect for Persons**, which is ensured by obtaining informed consent, consideration of privacy, confidentiality, and additional protections for vulnerable populations.
- 2) **Beneficence**, which is ensured by maximization of possible benefits and minimization of possible risks to all human subjects.
- 3) **Justice**, which is ensured by the equitable selection of subjects.

The Baystate HRPP, in partnership with the research community, is responsible for ensuring the ethical and equitable treatment of all human subjects in research conducted under its auspices.

1.5 Regulatory Compliance

The HRPP is responsible for ensuring compliance with federal regulations, state law and institutional policies. All human subjects research at Baystate is conducted in accordance with the policy and regulations found in the Common Rule and 21 CFR 50 and 56. The actions of Baystate will also conform to all other applicable federal, state, and local laws and regulations.

Baystate voluntarily applies the International Conference on Harmonization (“ICH”) Good Clinical Practices (“GCP”) Guidelines (sometimes referred to as “ICH-GCP” or “E6”) to certain types of human subjects research conducted under its HRPP. In general, Baystate applies the ICH-GCP guidelines only to the extent that they are compatible with FDA and DHHS regulations. See the document “International Conference on Harmonization (ICH) Good Clinical Practices (GCP), Applicability to Human Subjects Research” for guidance on the applicability of the ICH-GCP requirements.

1.6 Federalwide Assurance (FWA)

The HRPP operates under the authority of its Federalwide Assurance (FWA 00004355) and has designated two IRBs (IRB #1 is individually identified as IRB00002570 and IRB #2 as IRB00006178. with the Office of Human Research Protection (OHRP) to review all human research protocols.

In its FWA, Baystate has opted to limit the application of the FWA to research funded by DHHS or federal agencies that have adopted the Common Rule.

1.7 Research Covered by the HRPP

The Baystate HRPP covers all research involving human subjects that is under the auspices of Baystate. The research may be externally funded, funded from Baystate sources, or conducted without direct funding.

1.8 Written policies and procedures

The Baystate Standard Operating Policies and Procedures for Human Research Protection detail the policies and regulations governing research with human subjects and the requirements for submitting research proposals for review by the Baystate IRB. This is not a static document. The policies and procedures are under continuous oversight and are reviewed and if necessary revised at least annually by the Director of the HRPP with the input of the Institutional Review Board and the Research Integrity Officer. The IO reviews and approves all revisions of the policies and procedures.

The Director of the HRPP keeps the Baystate research community apprised of new information that may affect the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues on its website, through educational offerings, and via e-mail. The policies and procedures are available on the Baystate intranet and copies are provided on request. Changes to the policies and procedures are communicated to investigators, research staff, IRB members, and HRPP and IRB staff via e-mail and by posting to the website.

1.9 HRPP Organization

The HRPP is a comprehensive system to ensure the protection of human subjects participating in research. It consists of various of individuals and committees such as: the Institutional

Official, the Director of the HRPP, the Research Integrity Officer, the IRB, other committees or subcommittees addressing human subjects protection (e.g., Biosafety, Safety, Conflict of Interest), investigators, HRPP and IRB staff, research staff, health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer) and research pharmacy staff. The objective of this system is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

The following officials, administrative units and individuals have primary responsibilities for implementing the HRPP:

1.9.1 Institutional Official

The ultimate responsibility of the HRPP resides with the **Institutional Official (IO)** for research. The IO is responsible for ensuring the Baystate HRPP has the resources and support necessary to comply with all institutional policies and with federal regulations and guidelines that govern human subjects research. The IO is legally authorized to represent the Institution and is the signatory of the FWA and assumes the obligations of the FWA.

The IO also holds ultimate responsibility for:

- oversight of the Institutional Review Board (IRB);
- oversight over the conduct of research conducted by all BH investigators;
- assuring the IRB members are appropriately knowledgeable to review research in accordance with ethical standards and applicable regulations;
- assuring that all investigators are appropriately knowledgeable to conduct research in accordance with ethical standards and applicable regulations;
- Oversight of the development and implementation of an educational plan for IRB members, staff and investigators.

The IO is responsible for the final institutional approval of all research at Baystate. The IO may not approve any research involving human subjects that has not been approved by the IRB. The IO may disallow any research at Baystate regardless of approval by any IRB or any other institutional or outside approvals.

1.9.2 Director of the HRPP

The Director of the HRPP (Director) is appointed by and reports to the IO and is responsible for:

1. Developing, managing and evaluating policies and procedures that ensure compliance with all state, and federal regulations governing research. This includes monitoring changes in regulations and policies that relate to human research protection and overseeing all aspects of the HRPP program.
2. Advising the IO on key matters regarding research at Baystate.
3. Implementing the institution's HRPP policy.

4. Submitting, implementing and maintaining an approved FWA through the IO and the Department of Health and Human Services Office of Human Research Protection (OHRP).
5. Managing the finances of the Baystate HRPP.
6. Assisting investigators in their efforts to carry out the institution's research mission.
7. Developing and implementing needed improvements and ensuring follow-up of actions, as appropriate, for the purpose of managing risk in the research program.
8. Developing training requirements as required and as appropriate for investigators, committee members and research staff, and ensuring that training is completed on a timely basis.
9. Developing and implementing appropriate monitoring procedures for research involving human subjects.
10. Serving as the primary contact at Baystate for the Office for Human Research Protections (OHRP) of the U.S. Department of Health and Human Services, the Food & Drug Administration, and other regulatory agencies and accrediting bodies.
11. Day-to-day responsibility for the operation of the HRPP office, including supervision of HRPP and IRB staff.
12. Responding to faculty, student and staff questions.
13. Development of policy and procedures.
14. Organizing and documenting the review process.

1.9.3 Medical Director of the HRPP

The Medical Director of the HRPP (Medical Director) is a member of the medical faculty/medical staff, and has extensive knowledge and experience in the area of human subjects protection. The Medical Director currently serves as the IO, works collaboratively with the HRPP Director, and is responsible for assisting with implementation of the HRPP, including:

1. Serving as the physician liaison for the HRPP;
2. Serving as a resource to investigators in their efforts to carry out BH's research mission;
3. Assisting in the development of and approving HRPP policies and procedures;
4. Reviewing findings from the research QA/QI program and IRB-approved corrective action plans;
5. Providing consultation and support to the IRB Chairs and HRPP Director, as needed;
6. Ensuring that IRB approved protocols are conducted in accordance with approved procedures, and that periodic monitoring occurs;
7. Making recommendations regarding the development of education and training requirements for investigators, IRB members and research staff;

8. Conducting educational and faculty development seminars for investigators on the conduct of research and research ethics;
9. Fostering communication among the IRB and other BH offices or committees as appropriate to enhance a cohesive approach to research involving human subjects;
10. Ensuring quality assurance/quality improvement activities for the IRB and HRPP; Reviewing findings from the research QA/QI program and IRB-approved corrective action plans and contributing as appropriate;
11. Ensuring that the institution's reporting obligations to sponsors and federal regulatory agencies are fulfilled.

1.9.4 Research Integrity Officer

The Research Integrity Officer (RIO) is appointed by and reports to the IO and is responsible for:

1. Advising the IO on matters involving compliance of research and scholarly activities at the Institution.
2. Serving as a resource on matters related to human subjects research to the HRPP, IRB, IBC, IACUC, and SPA.
3. Providing review of research policies, procedures, and practices to ensure compliance with regulations and guidance.
4. Overseeing the process and ensuring compliance with the Policy on Scientific Misconduct in Research and Scholarly Activities.
5. Monitoring policies and procedures regarding financial disclosures and research conflict of interest and coordinating implementation with the Institution's Corporate Compliance Department.
6. Implementing reviews and plans to resolve issues related to noncompliance in cooperation with the Directors and the IRBs.
7. Providing guidance on Massachusetts law, local ordinances and the laws of any other jurisdiction where research is conducted as they apply to research, in consultation with the attorneys of the firm designated as General Counsel to the Institution.

1.9.5 Institutional Review Board (IRB)

Baystate has two on-site IRBs (hereafter, *the IRB*), each with Chairs and members appointed by the IO. Each IRB is a "general" IRB, meaning that it conducts reviews of all categories of human subjects research. The IRBs are autonomous administrative bodies established to protect the rights and welfare of human research subjects who participate in research activities conducted under the auspices of BH. The IRB prospectively reviews and makes decisions concerning all

human research conducted at its facilities or by its employees or agents, or under its auspices. The IRBs discharge these duties by complying with the requirements of the Common Rule; the Food & Drug Administration (FDA); federal and state regulations, the FWA; and institutional policies. (See Section 2 for a detailed discussion of the IRB.)

1.9.6 Counsel

The Baystate HRPP relies on an attorney for the interpretations and applications of Massachusetts law and the laws of any other jurisdiction where research is conducted as they apply to human subjects research. The Institutional Official (IO) arranges for appropriate legal counsel. Legal counsel may consist of BMC staff or outside counsel.

1.9.7 Department Chairs

Department Chairs are responsible for ensuring that the Principal Investigator (PI) is qualified by training and experience to conduct the proposed research. In addition, Department Chairs are responsible for ensuring that the PI has sufficient resources and facilities to conduct the proposed research in a way that will protect the rights and welfare of participants. Such resources include but are not necessarily limited to personnel, space, equipment and time. For each protocol submitted to the BMC IRB for approval, the Department Chair or their designee must certify that s/he accepts responsibility for assuring adherence to the federal and state regulations and institutional policies governing the protection of human subjects of research, including applicable institutional credentialing requirements.

Department Chairs are required to establish a review process for all proposals before they are submitted to the IRB for review. The signature of the Department Chair or designee indicates that the study has scientific merit, that the design is such that it can reasonably be expected to answer the proposed question, and that the PI, with other investigators and staff, has sufficient resources and ability to conduct the research.

1.9.8 The Principal Investigator

The Principal Investigator (PI) is the ultimate protector of the human subjects who participate in research. The Principal Investigator is ultimately responsible for all aspects of the study and shall assure that all activities of the study and that all investigators and staff comply with all institutional, federal, and state requirements and guidelines. The Principal Investigator shall abide by the highest ethical standards and develop a protocol that incorporates the principles of the Belmont Report. The Principal Investigator is expected to conduct research in accordance with the approved research protocol and to oversee all aspects of the research by providing supervision of the research team, including oversight of the informed consent process. All subjects must give informed consent to participate unless this requirement is waived by the IRB and the investigator must establish and maintain an open line of communication with all research subjects within his/her responsibility. In addition to complying with all the policies and standards of the governing regulatory bodies; the investigator must comply with institutional and administrative requirements for conducting research. The

investigator is responsible for ensuring that research staff complete appropriate training and must obtain all required approvals prior to initiating research. When investigational drugs or devices are used and the services of the Investigational Pharmacy are not engaged, the investigator is responsible for providing written procedures for their storage, security, dispensing and disposal. Such procedures must be approved by the HRPP.

1.9.9 Other Related Units

1.9.9.1 Epidemiology and Biostatistics Research Core

The Epidemiology and Biostatistics Research Core (EBRC) is a core unit within Academic Affairs, which provides methodologic and analytic support to Baystate faculty and clinicians undertaking clinical research.

The EBRC has three broad functions:

- 1) **Research Support:** Staff members collaborate with clinical investigators in designing and analyzing ongoing and new research initiatives. Support activities include study design and protocol development, power analysis and sample size estimation, writing methodology and analytic sections for grants, manuscripts, and presentations.
- 2) **Education in Research Methods:** The EBRC helps advance the skills and knowledge of clinical faculty in research methodology through education and practice. Staff members conduct regular seminar series on study design, survey and questionnaire design, and interpretation of statistical analyses.
- 3) **Review of study protocols for the IRB:** The staff of the EBRC review the design and analysis of all investigator-initiated protocols from BMC clinical faculty that are submitted to the IRB. Problems identified in the protocol review are resolved by working collaboratively with the investigator to revise the protocol.

1.9.9.2 Sponsored Programs Administration

The Sponsored Programs Administration (SPA) office is charged with providing the Baystate Medical Center (BMC) community with pre-award and post-award administrative support for both internal and external sponsored projects. The office provides institutional review and endorsement for proposals; reviews and negotiates award agreements; requests the establishment of new project activities; prepares subawards and subcontracts; provides post-award business and financial assistance, advice, and approvals; and performs compliance training and other activities for adherence to Baystate and sponsor regulations. SPA aids Finance in close-outs of awards and prepares financial reports for Academic Affairs.

Any formal proposal requesting project support for Baystate Health (research or otherwise) from an external funding organization must be approved before it is submitted to the funding organization. Approval for these submissions must be routed through SPA if it involves

requesting funds from extramural sources for the purpose of supporting public service, research, or educational functions at or by Baystate Health with a deliverable product or service and uses Baystate Health resources (personnel, facilities, equipment, etc.) regardless of whether or not an institutional signature is required by the sponsor.

Proposals that meet this definition include initial submissions as well as renewals, continuations, and/or revisions. Funding organizations include all federal, state, county or local government agencies; foundations; non-profit organizations; private corporations; colleges and universities, and any other private or public group that awards grants to hospitals for the performance of a specific scope of work.

SPA balances the facilitation of research for the Baystate Health community with institutional compliance for externally funded research, educational, and public service projects in collaboration with other divisions in Academic Affairs; BMC Human Resources and Finance Offices; and Department Chairs and individual Investigators.

1.9.9.3 Baystate Pharmacy

A pharmacist from Baystate serves on the IRB, providing expertise to the IRB and allowing the Pharmacy to have complete information about all IRB approved research that takes place at Baystate and under its jurisdiction.

The Pharmacy provides the services of an Investigational Drug Service (IDS). General responsibilities of the IDS office include but are not limited to the ordering, handling, inventorying, and dispensation of study/investigational medications, creating randomization schemes, randomizing participants, and adhering to all FDA requirements via Hospital established quality assurance and sponsor and governmental audits.

When the services of the IDS are not engaged, the investigator is responsible for adhering to regulations and Institutional policies and procedures regarding drug storage, security, dispensing and disposal.

1.9.9.4 Institutional Biosafety Committee:

The Baystate Medical Center (BMC) Institutional Biosafety Committee (IBC) is comprised of scientists, physicians, safety professionals and community members who are responsible for reviewing a wide range of research activities that may pose a potential risk to public health or the environment. Ad hoc consultants are utilized by the committee as needed.

All research conducted by BMC employees or students involving any of the agents or materials listed below must be approved by the BMC Institutional Biosafety Committee (IBC) prior to initiation:

- Hazardous biological agents (mostly BSL2, BSL3, and BSL4 agents) of humans, animals, or plants

- “Dual Use” (see www.biosecurityboard.gov/links.asp) or potential biological weapons or drug resistance enhancements including HHS and USDA Select Agents and Toxins (see <http://www.selectagents.gov/Select%20Agents%20and%20Toxins%20List.html>)
- Any material requiring a CDC import license or a USDA permit
- Recombinant DNA or RNA including creation or use of transgenic plants and animals,
- Transfer of recombinant DNA or biological agents containing recombinant DNA into human subjects
- Radiological hazards
- Carcinogenic, toxic, or acutely hazardous chemicals

1.9.10 Relationship Between Components

The IRB functions independently of, but in coordination with, other individuals and committees within the institution. The IRB, however, makes its independent determination whether to approve or disapprove a protocol based upon whether or not human subjects are adequately protected. The IRB has review jurisdiction over all research involving human subjects conducted, supported, or otherwise subject to regulation by any federal department or agency that has adopted the human subjects regulations.

The **Research Council** meets at a minimum of annually to ensure a dialogue is maintained between the various entities involved in the oversight and approval of research at Baystate. Membership is comprised of the following individuals or their designees: the Research Integrity Officer, the HRPP Director, the Director of SPA, the Director of the EBRC, the Chairs of the IRBs, the Chair of IACUC, the Vice President of Patient Care Services, the Director of Safety and Environmental Affairs, the Chair of IBC, the Director of Pharmacy, the Chairman of Pathology, and representatives from Medical Records and Information Services with the IO as Chair. The committee serves in an advisory capacity to the IO, monitoring the effectiveness of existing programs, developing new or revised policies as changes in requirements occur, and disseminating updated compliance information to the research community.

The **Principal Investigator Advisory Committee** informs and advises the IO about issues related to research infrastructure and support. The Committee charge is to identify obstacles and help develop solutions to support investigators in the conduct of their research at Baystate. The Committee membership includes representatives of research leadership from the clinical departments. The Principal Investigators Advisory Committee meets at a minimum of semiannually.

Research that has been reviewed and approved by the IRB is subject to review and disapproval by other officials of the institution for other components of the study. The IO is responsible for the final institutional approval of all research at Baystate. The IO may not

approve any research involving human subjects or PHI that has not been approved by the IRB. The IO may disallow any research at Baystate regardless of approval by any IRB or any other institutional or outside approvals.

1.9.10.1 Protocol-specific coordination

The HRPP utilizes IRBNet to facilitate on-line coordination and documentation of protocols including the communication, review, and, where required, electronic signatures, of the various components of the institution necessary to indicate institutional support for the research.

The initial electronic submission of all research projects is to Sponsored Programs Administration (SPA). This submission serves as the institutional registration of the project and allows SPA to determine if its services are required for the proposed research.

Electronic signature requirements for initial submissions to the IRB include the:

- Principal Investigator
- Each member of the research team
- Ancillary services as applicable to the research (i.e., Pathology, Investigational Drug Services, Radiology, Nursing)
- Additional Individuals and Committees as applicable to the research (i.e., IBC, Safety, Radiation Safety, the Dean)
- The Department Chair (or equivalent) or designee
- Other Department Chairs when the research overlaps departments

1.10 HRPP Operations

1.10.1 HRPP Office

The Baystate HRPP Office reports directly to the IO and is supervised by the Director of the HRPP (Director). The Director has expert knowledge in regulatory issues regarding human subjects and serves as the Human Protections Administrator and is the primary contact at Baystate for the Office for Human Research Protections and the Food & Drug Administration. The Medical Director of the HRPP (Medical Director) is a member of the medical faculty/medical staff, and has extensive knowledge and experience in the area of human subjects protection. The Medical Director currently serves as the IO, works collaboratively with the HRPP Director, and is responsible for assisting with implementation of the HRPP.

The Director of the HRPP has day-to-day responsibilities for the operation of the IRBs. This includes responding to questions about human subjects research as well as organizing and documenting the review process. The Director works closely with the Institutional Official (IO),

Research Integrity Officer (RIO), and the Chairs of the IRBs in the development of policy and procedures. Additionally, the office is staffed by IRB Analysts, IRB Coordinators, and Integrity and Education Specialists. The duties and responsibilities for all staff are found in their respective job descriptions, and their performance is evaluated on an annual basis.

1.10.2 IRB Analyst

The IRB Analyst functions under the supervision of the HRPP Director and is responsible for implementing and coordinating the daily activities of the IRB including providing support to the HRPP Directors, the IRB Chairs, and IRB Members.

The IRB Analyst functions as a resource to research investigators and staff. The IRB Analyst is responsible for providing clear and accurate instructions, guidance, and support to researchers through the entire regulatory process. This includes assistance in creating successful and compliant applications for Institutional Review Board (IRB) review and support of best practices in research and adherence to research regulations, policies, and guidelines. The IRB Analyst is responsible for conducting an initial review of all submissions to the IRB for completeness, accuracy, and regulatory compliance. The IRB Analyst is responsible for ensuring the completeness and accuracy of IRB records. The IRB Analyst develops the IRB minutes and reviews them for accuracy, and ensures proper documentation of discussions including controverted discussions and actions taken by IRB during convened meetings.

1.10.3 IRB Coordinator

The IRB Coordinator functions under the supervision of the HRPP Director and is responsible for implementing and coordinating the daily activities of the IRB including providing support to the HRPP Directors, the IRB Analysts, the IRB Chairs, and IRB Members.

The IRB Coordinator functions as a resource to research investigators and staff. The IRB Coordinator is responsible for providing clear and accurate instructions, guidance, and support to researchers through the entire regulatory process including support of best practices in research and adherence to research regulations, policies, and guidelines. The IRB Coordinator is responsible for conducting an initial review of all submissions to the IRB for completeness and accuracy. The IRB Coordinator is responsible for ensuring the completeness and accuracy of IRB records. The IRB Coordinator contributes to the development of the IRB minutes.

1.10.4 HRPP Integrity and Education Specialist

The HRPP Integrity & Education Specialist reports to the HRPP Director and is responsible for providing training in the various aspects of review and conduct of human subjects research in support of best practices and adherence to research regulations, policies, and guidelines. This position acts as an integrity navigator for human subjects' research. The HRPP Integrity & Education Specialist mentors researchers and research staff through the process of study development and the conduct of the study after IRB approval. This mentoring will provide practical, hand-on advice in a supportive and collegial atmosphere.

The HRPP Integrity / Education Specialist will also monitor compliance in the conduct of studies and the IRB with institutional, state, and national regulations, policies, and guidelines for human subjects' research, including periodic reports to the HRPP Directors, the IRB, the Research Integrity Officer (RIO), and the Institutional Official.

1.11 HRPP Resources

The HRPP Office, is located in offices at Baystate and is equipped all necessary office space, meeting space, storage space and equipment to perform the functions required for the HRPP. The adequacy of personnel and non-personnel resources of the HRPP program is assessed on an annual basis by the Director with the HRPP staff and is reviewed and approved by the IO.

The Baystate Institutional Official (IO) assures adequate resources to the IRB and HRPP Office, including adequate meeting and work space, staff, office equipment and supplies, file cabinets, computers, internet access, and copiers. The resources provided for the IRB and HRPP Office are reviewed during the annual budget review process.

1.12 Conduct of Quality Assurance/Quality Improvement Activities for IRB Operation

The objective of Baystate's HRPP Quality Assurance / Quality Improvement Plan is to measure and improve human research protection effectiveness, quality, and compliance with organizational policies and procedures and applicable federal, state, and local laws. The Quality Assurance / Quality Improvement Plan is managed and implemented by the HRPP Director in collaboration with the Research Integrity Officer.

1.12.1 Research Compliance Reviews

Directed ("for cause") and periodic compliance ("not for cause") reviews are conducted to assess investigator compliance with federal, state, and local law, and Institution policies, and to identify areas for improvement, and suggest recommendations based on existing policies and procedures. Directed reviews of IRB-approved research studies are in response to identified concerns. Periodic ("not for cause") reviews are conducted using a systematic method to review IRB-approved research on a regular basis. The results are reported to the Director and the IRB Chair.

Activities of reviewers during directed and periodic compliance reviews may include:

- a) Requesting progress reports from researchers;
- b) Examining investigator-held research records;
- c) Contacting research subjects;
- d) Observing research sites where research involving human research subjects and/or the informed consent process is being conducted;
- e) Review of advertisements and other recruiting materials;

- f) Reviewing projects to verify from sources other than the researcher that no unapproved changes have occurred since previous review;
- g) Monitoring conflict of interest concerns to assure the consent documents include the appropriate information and disclosures;
- h) Monitoring HIPAA authorizations;
- i) Comparison of published reports of research to IRB records
- j) Conducting other monitoring activities as deemed appropriate by the IO, the RIO, the Director, and the IRB.

1.12.2 Research Compliance Reviews of External Sites

Directed (“for cause”) and periodic (“not for cause”) compliance reviews are conducted at non-Baystate sites, where Baystate’s IRBs serve as the “IRB of Record,” to assess compliance with federal, state, and local law, research subject safety, and HRPP policies and procedures. These reviews may include items listed in section 1.15.1 above.

1.12.3 Audits and Inspections by External Agencies and Others

The HRPP and all potentially affected ancillary services (for example, investigational pharmacy) must be notified immediately when investigators receive an audit or inspection announcement from a regulatory agency. The HRPP will assist the investigator in preparing for such audits and may attend entrance and exit interviews. All reports from regulatory audits must be submitted to the HRPP, Department Chair, the Institutional Official or designee, and affected ancillary services promptly. When applicable, the HRPP will assist in preparing a response to the findings and will provide a report to the IRB.

The HRPP and all potentially affected ancillary services must be notified promptly when investigators receive an audit announcement by other external groups such as sponsors and cooperative groups. The HRPP may assist the investigator in preparing for such audits and may attend entrance and exit interviews. All reports from such audits must be submitted to the HRPP, Department Chair, Institutional Official and affected ancillary services promptly. When applicable, the HRPP will assist in preparing a response to the findings and will provide a report to the IRB.

In the event the IRB is audited by an external regulatory agency, the IRB will immediately notify the Institutional Official and all other appropriate persons within the institution. The IRB will provide the regulatory agency with full access to all requested information and will be fully responsive to required actions.

1.12.4 Reporting and Disposition

The results of research quality assurance activities are reported to the Director and the IRB Chair. Any noncompliance is managed according the procedures in Section 11 of these Policies and Procedures.

If an audit or review finds that subjects in a research project have been exposed to unexpected serious harm, the reviewer will promptly report such findings to the RIO, the Director and the IRB Chair for immediate action.

1.12.5 IRB Compliance Reviews

Directed and random compliance reviews of the IRB are conducted. The results may affect current practices and may require additional educational activities, and are reported to the Director. The HRPP Integrity and Education Specialist will:

- a) Assess the IRB minutes to determine that adequate documentation of the meeting discussion has occurred. This review includes assessing the documentation surrounding the discussion for protections of vulnerable populations as well as other risk/benefit ratio and consent issues that are included in the criteria for approval;
- b) Assess the IRB minutes to assure that quorum was met and maintained;
- c) Assess the adequacy of documentation of the review of unanticipated problems, complaints, and protocol deviations and violations;
- d) Assess that privacy provisions, including HIPAA authorization; have been adequately reviewed, discussed and documented;
- e) Assess the documentation of continuing review to verify substantive and meaningful review and that no lapse has occurred since the previous IRB review;
- f) Observe IRB meetings or other related activities;
- g) Review IRB files to assure retention of appropriate documentation and consistent organization;
- h) Review of worksheets and Reviewer Comments by the IRB members;
- i) Verify IRB approvals for collaborating institutions or external performance sites;
- j) Perform other monitoring activities deemed appropriate by the IO, the RIO, the Director, and the IRB.

1.12.6 HRPP Compliance Reviews

The Institutional Official may direct the Research Integrity Officer to conduct or oversee a compliance review of the HRPP as a whole or of any of its components. The results may impact current practices and may require additional educational activities, and are reported to the Institutional Official and the Director of the HRPP.

1.12.7 Quality Improvement

Quality assurance reports, including compliance reviews, are reviewed by the Director, with the RIO and the Institutional Official available for consultation, in order to identify trends and to determine if systemic changes are required to prevent re-occurrence. If so, the Director, the

RIO, and the Institutional Official will collaborate in the development of a corrective action plan, its implementation, and evaluation of its effectiveness.

Quality assurance reports of the HRPP are reviewed by the Research Integrity Officer and the Institutional Official. If systematic changes are required in the HRPP, the Director, the RIO, and the Institutional Official will collaborate in the development of a corrective action plan, its implementation, and evaluation of its effectiveness.

1.13 Collaborative Research Projects

In the conduct of collaborative research projects, Baystate acknowledges that each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with applicable federal regulations. When a cooperative agreement exists, Baystate may enter into a joint review arrangement, rely on the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort. A formal relationship must be established between Baystate and the other institution through either a Cooperative Agreement or a Memorandum of Understanding that is approved by the IO or designee. This relationship must be formalized before Baystate will accept any human research proposals from the other institution or rely on the review of the other institution.

It is the policy of Baystate to assure that all facilities participating in a human subjects study receive adequate documentation about the study in order to protect the interests of study participants. Before a study can begin, it must be approved by the IRBs of record for each participating facility and, where appropriate, the IRB of record for the coordinating facility.

For collaborative research where the Baystate PI is the lead PI or Baystate is the coordinating center, the PI must identify all institutions participating in the research, the responsible IRB(s), and the procedures for dissemination of protocol information (IRB initial and continuing approvals, relevant reports of unanticipated problems, protocol modifications, and interim reports) between all participating institutions.

When Baystate relies on another IRB, the Director of the HRPP Office reviews the policies and procedures of the IRB to ensure that they meet Baystate standards. If the other IRB is part of an accredited HRPP, it is expected that Baystate standards are being met.

When Baystate reviews research conducted at another institution, the particular characteristics of each institution's local research context must be considered, either (i) through knowledge of its local research context by the Baystate IRB or (ii) through subsequent review by appropriate designated institutional officials, such as the Chairperson and/or other IRB members.

If Baystate is the coordinating facility, the Principal Investigator must document how the important human subject protection information is communicated to the other participating facilities engaged in the research study. The Principal Investigator is responsible for serving as the single liaison with outside regulatory agencies, with other participating facilities, and for all aspects of internal review and oversight procedures. The Principal Investigator is responsible

for ensuring that all participating facilities obtain review and approval from their IRB of record and adopt all protocol modifications in a timely fashion. The Principal Investigator is responsible for ensuring that the research study is reviewed and approved by any other appropriate committees at the coordinating facility and at the participating facilities prior to enrollment of participants.

The PI must follow these procedures when the Baystate PI is the lead investigator or Baystate is the coordinating facility of a multi-site study:

- In the initial IRB submission, the investigator indicates within the application that Baystate is the coordinating facility of a multi-site study.
- The investigator submits the following information in their IRB application materials:
 - Sufficient information to determine whether research activities at participating institutions result in the institution being engaged in research
 - Name of each participating facility
 - Confirmation that each participating facility has an FWA (including FWA number)
 - Contact name and information for investigator at each participating facility
 - Contact name and information for IRB of record at each participating facility
 - Method for assuring all participating facilities have the most current version of the protocol
 - Method for confirming that all amendments and modifications in the protocol have been communicated to participating sites
 - Method for communicating to participating facilities any serious adverse events and unanticipated problems involving risks to subjects or others
 - Method of communicating regularly with participating sites about study events
- The investigator submits approval letters from all the IRBs of record for all participating sites.
- The investigator maintains documentation of all correspondence between participating sites and their IRBs of record.

2 Institutional Review Board

Baystate has established an Institutional Review Board (IRB) to ensure the protection of human subjects in human subjects research conducted under the auspices of Baystate. All non-exempt human subjects research conducted under the auspices of the Baystate must be reviewed and approved by the Baystate IRB prior to the initiation of the research.

Although Baystate has authorized more than one IRB to fulfill this function, all Baystate IRBs follow these same policies and procedures. Therefore, for the purposes of this document, all Baystate IRBs are referred to as the Baystate IRB.

The Baystate IRB may serve as the IRB of record for research conducted at other institutions under special agreement. The IO and HRPP Director will consider such requests to serve as the IRB of record on an individual basis. Fees may be charged as appropriate to cover the costs associated with taking on such a responsibility. When the Baystate IRB is the IRB of record, the research is subject to these policies.

Baystate also utilizes the services of the NCI Adult CIRB for Radiation Therapy Oncology (RTOG) protocols; and on occasion, as determined appropriate by the HRPP Director, enters into agreement to cede authority to a non-local IRB

The authorized off-site IRBs that serve as the IRB-of-record for Baystate have the same authority as the on-site IRB and all determinations and findings of the off-site IRBs are equally binding on all research under the auspices of the institution..

The following describes the authority, role and procedures of the on-site IRBs.

2.1 IRB Authority

Under the Federal Regulations and institutional policy, the IRBs authority includes:

1. To approve, require modifications to secure approval, defer, or disapprove all human subjects research activities overseen and conducted under the auspices of BH, regardless of location of the research activities;
2. To suspend or terminate approval of research not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to participants;
3. To observe, or have a third party observe, the consent process; and
4. To observe, or have a third party observe, the conduct of the research.

No research involving human subjects may commence until all required Institutional approvals (including IRB) are obtained. Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of the institution. However, those officials may

NOT approve the implementation of research if it has not been approved by the IRB nor may those officials override the decision of the IRB. Institution officials may strengthen requirements and/or conditions, or add other modifications to secure institutional approval or approval by another institution committee. Previously approved research proposals and/or consent forms must be re-approved by the IRB before initiating the changes or modifications. The IRB Chair or designee makes the determination whether the changes require full IRB review or expedited review.

2.2 Number of IRBs

There are currently two on-site IRBs and multiple off-site IRBs including the National Cancer Institute Adult Central IRB (NCI CIRB) and other IRBs under special agreement as determined appropriate by the IO or designee. The on-site IRBs are generalist IRBs responsible for the review of all types of research conducted at the organization. The NCI CIRB is utilized for Radiation Therapy Oncology Group Protocols under the process of facilitated review; the responsibilities for review and oversight by other off-site IRBs are determined on an individual basis and documented via an Institutional Agreement. The IO, the Director, and the Chair of the IRB will review the activity of the on-site IRBs on at least an annual basis and make a determination as to the appropriate number of IRBs that are needed for the institution. The utilization of and performance of the off-site IRBs will also be evaluated on an annual basis.

2.3 Roles and Responsibilities

2.3.1 Chair of the IRB

The leadership positions of Chair and Vice Chair of an IRB are appointed by the Institutional Official to serve for renewable three-year terms subject to reappointment or removal as determined solely by the Institutional Official. A Chair or Vice Chair may be appointed to a leadership position on more than one IRB.

The IRB Chair should be a highly respected individual, from within Baystate, fully capable of managing the matters brought before the IRB with fairness and impartiality. The task of making the IRB a respected part of the institutional community will fall primarily on the shoulders of the Chair. The IRB must be perceived to be fair, impartial and immune to pressure by the institution's administration, the investigators whose protocols are brought before it, and other professional and nonprofessional sources.

The IRB Chair is responsible for conducting the meetings of the IRB and other responsibilities as described within these policies and the regulations governing the conduct of human subjects research. This includes the designation of other experienced members of the IRB to conduct exempt and expedited reviews and other functions. The IRB Chair or his/her designee builds collegial relationships with investigators and Department Chairs through active communication on both protocol-specific and general issues as related to human subjects protections. The IRB Chair(s) take an active role in the education of the research community and contribute to the development of human subjects research policies and guidance.

The IRB Chair and the Director advise the Institutional Official regarding IRB member performance and competence.

The performance of IRB Chair is reviewed on an annual basis by the Institutional Official in consultation with the Director and feedback is given to the Chair. If the Chair is not acting in accordance with the IRB's mission, following these policies and procedures, has an undue number of absences, or not fulfilling the responsibilities of the Chair, the Chair may be removed by the Institutional Official.

2.3.2 Vice Chair of the IRB

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

2.3.3 Subcommittees of the IRB

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

If the IRB Chair creates one or more IRB Subcommittees, he/she shall also indicate whether it is a standing or *ad hoc* IRB Subcommittee.

2.4 IRB Membership

IRB members are selected based on appropriate diversity, including consideration of race, gender, cultural backgrounds, specific community concerns in addition to representation by multiple, diverse professions, knowledge and experience with vulnerable subjects, and inclusion of both scientific and non-scientific members. The structure and composition of the IRB must be appropriate to the amount and nature of the research that is reviewed. Every effort is made to have member representation that has an understanding of the areas of specialty that encompasses most of the research performed at Baystate. Baystate has procedures that specifically outline the requirements of protocol review by individuals with appropriate scientific or scholarly expertise.

In addition, the IRB will include members who are knowledgeable about and experienced working with the vulnerable populations that typically participate in Baystate research.

Individuals from Baystate's Financial Administration, Sponsored Programs Administration, or Office of Technology Transfer may not serve as members of the IRB or carry out day-to-day operations of the IRB review process. Individuals from these offices may provide information to the IRB and attend IRB meetings as guests.

The IRB must promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects; and possess the professional competence necessary to review specific research activities. A member of the IRB may fulfill multiple membership position requirements for the IRB.

2.5 Composition of the IRB

1. The IRB will have at least five members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution.
2. The IRB is sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.
3. In addition to possessing the professional competence necessary to review specific research activities, The IRB is able to ascertain the acceptability of proposed research in terms of institutional policies and regulations, applicable law, and standards of professional conduct and practice. The IRB will therefore include persons knowledgeable in these areas.
4. If the IRB regularly reviews research that involves a vulnerable category of subjects (e.g., children, prisoners, pregnant women, or handicapped or mentally disabled persons), consideration is given to the inclusion of one or more individuals on the IRB who are knowledgeable about and experienced in working with these subjects. When protocols involve vulnerable populations, the review process will include one or more individuals who are knowledgeable about or experienced in working with these participants, either as members of the IRB or as consultants.
5. Every nondiscriminatory effort is made to ensure that the IRB does not consist entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. The IRB shall not consist entirely of members of one profession.
6. The IRB includes at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.
7. The IRB includes at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

8. The IRB includes at least one member who represents the general perspective of research participants.
9. One member may satisfy more than one membership category.
10. The Directors and staff of the HRPP and IRB offices may be voting members of the IRB.

2.6 Appointment of Members to the IRB

Members of the IRB are appointed by the Institutional Official or designee. The IRB Chair and/or the Director of the HRPP are responsible for advising the Institutional Official on the need to expand membership or replace an outgoing member or alternate. The Institutional Official will consider recommendations received from the Director of the HRPP, IRB Chairs, IRB members, Department Chairs, Program Directors, and others.

Potential members are contacted by the Director of the HRPP or the IRB Chair to discuss the role and expectations of an IRB member and to solicit information regarding the nominee's qualifications.

Appointments are made for a renewable three-year period of service. An appointment, reappointment, or any change in status such as removal, must be provided in writing. A Member may resign by providing written notification to the Director of the HRPP or the IRB Chair.

On an annual basis, the Institutional Official and the Director of the HRPP review the membership and composition of each IRB to determine if they continue to meet regulatory and institutional requirements. Changes to IRB membership will be reported to OHRP within 90 days.

2.7 Alternate Members

The appointment and function of alternate members is the same as that for primary IRB members. The alternate's expertise and perspective are expected to be comparable to those of the primary member. The role of the alternate member is to serve as a voting member of the IRB when the regular member is unavailable to attend a convened meeting. When an alternate member substitutes for a primary member, the alternate member will receive and review the same materials prior to the IRB meeting that the primary member received or would have received.

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

Experienced Alternate members may perform expedited reviews if so delegated by the IRB Chair.

Alternate members are expected to attend or observe a minimum of two IRB meetings per year.

2.8 IRB Member Conflict of Interest

No IRB member may participate in the review (initial, continuing, or modification) of any research project in which the member has a conflict of interest (COI), except to provide information as requested. It is the responsibility of each IRB member or HRPP/IRB staff member to disclose any COI in a study submitted for review and recuse him/herself from the processing, deliberations, and votes. For convened board review, the conflicted member or staff must leave the meeting room.

All voting members of the IRB complete a corporate Conflict of Interest disclosure when first appointed and at a minimum of annually thereafter. If a member responds affirmatively to the existence of a potential conflict, the member will not be assigned to review of any protocols for which they may have a conflict.

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

1. Where the member or consultant is involved in the design, conduct, and reporting of the research.
2. Where an immediate family member of the member or consultant is involved in the design, conduct, and reporting of the research.
3. Where the member holds significant financial interests related to the research being reviewed.
4. Any other situation where an IRB member believes that another interest conflicts with his or her ability to deliberate objectively on a protocol.

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

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

2.9 Use of Consultants

When necessary, the IRB Chair or the HRPP Director may solicit individuals from the organization or the community with competence in special areas to assist in the review of issues or protocols, which require scientific or scholarly expertise beyond or in addition to that

available on the IRB. The need for an outside reviewer is determined in advance of the meeting by the HRPP Director or IRB Chair by reviewing the protocols scheduled to be reviewed at the convened meeting. IRB members may also request consulting opinions. The HRPP Office will ensure that all relevant materials are provided to the outside reviewer prior to the convened meeting.

Written statements of consultants are kept in IRB records. Key information provided by consultants at meetings is documented in the minutes. Written reviews provided by the outside reviewer are filed with the protocol.

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

The consultant's findings are presented to the full board for consideration either in person or in writing. If in attendance, these individuals will provide consultation but may not participate in or observe the vote.

Ad hoc or informal consultations requested by individual members (rather than the full board) are requested in a manner that protects the researcher's confidentiality and is in compliance with the IRB conflict of interest policy (unless the question raised is generic enough to protect the identity of the particular PI and research protocol).

2.10 Duties of IRB Members

The agenda, submission materials, protocols, proposed consent forms and other appropriate documents are distributed to members on-line prior to the convened meetings at which the research is scheduled to be discussed. Members are expected to review the materials prior to each meeting in order to participate fully in the review of each proposed project. IRB members will treat the research proposals, protocols, and supporting data confidentially. All printed copies of the protocols and supporting data are to be disposed of in a secured BH bin or shredded.

2.11 Attendance Requirements

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

If an IRB member is to be absent for an extended period of time, such as for a sabbatical, he or she must notify the IRB at least 30 days in advance so that an appropriate replacement can be obtained. The replacement can be temporary, for the period of absence, or permanent if the

member is not returning to the IRB. If the member has a designated alternate, the alternate can serve during the primary member's absence, provided the IRB has been notified in advance.

Alternate members are expected to attend or observe a minimum of two IRB meetings per year.

2.12 Training / Ongoing Education of Chair and IRB Members in Regulations, Procedures

A vital component of a comprehensive human research protection program is an education program for IRB Chair and members. Baystate is committed to providing training and an on-going educational process for IRB members and the staff of the HRPP Office, related to ethical concerns and regulatory and institutional requirements for the protection of human subjects.

Orientation

New IRB members, including alternate members, will meet with the IRB Chair or the Director of the HRPP or designee for an informal orientation session. At the session, the new member is provided with a copy of the "Institutional Review Board Member Handbook" (by Robert J. Amdur; Elizabeth A. Bankert) and provided directions to access additional materials such as these procedures, the Belmont Report, and federal regulations on-line.

New IRB members are expected to observe a minimum of one meeting and are required to complete the Initial Education requirements for IRB members before their appointment to the IRB becomes official; afterwards they may serve as Primary Reviewer. Members in training do not count towards quorum until training is complete.

Initial Education

New IRB members will complete the on-line modules in the PRIM&R ***Ethical Oversight of Human Subjects Research Course***. At the discretion of the Director, based upon the availability of the PRIM&R course or a new member's training and experience, the CITI Course in the Protection of Human Research Subjects may be substituted.

Continuing Education

To ensure that oversight of human research is ethically grounded and the decisions made by the IRB are consistent with current regulatory and policy requirements, training is continuous for IRB members. Educational activities include, but are not limited to;

- In-service training at IRB meetings;
- Training workshops;
- Copies of appropriate publications;

- Identification and dissemination by the HRPP Director or the HRPP Integrity and Education Specialist of new information that may impact the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues to IRB members via email, mail, or during IRB meetings;
- Unlimited access to the HRPP resource library.

The Organization will provide support to send as many members of the IRB as possible to attend the annual PRIM&R conference or regional conferences on human research protections.

The HRPP and IRB Office Staff are required to complete the CITI Course in the Protection of Human Research Subjects or alternate approved education. Staff are expected to attend PRIM&R or other training as delegated by the Director.

The IRB Office Staff are expected to become CIP or CIM-certified, or approved alternate certification, within a period of one year of eligibility.

2.13 Liability Coverage for IRB Members

Baystate maintains Directors and Officers insurance coverage for all persons serving on Baystate committees, including an IRB, acting within the scope of their duties. Through its program of self-insurance, Baystate Health Insurance Corporation, Ltd., Baystate provides general and professional liability insurance for all employees and authorized agents acting within the scope of their employment or authorization.

2.14 Review of IRB Member Performance

Performance of each IRB member and alternate member is reviewed on an annual basis by the Chair and Director of the HRPP Office and feedback is given to the member. Members who are not acting in accordance with the IRB's mission or policies and procedures or who have an undue number of absences shall be removed.

2.15 Reporting and Investigation of Allegations of Undue Influence

If an IRB Chair, member, or staff person has concerns that the IRB has acted in any manner that is inconsistent with institutional policies or federal guidelines, or has been unduly influenced by any party, the individual shall report this confidentially to the HRPP Director or Institutional Official. The Institutional Official is responsible for oversight of an appropriate investigation and, if a concern is validated, taking corrective actions to prevent additional occurrences. The investigation may include the HRPP Director, the RIO, or others as determined by the Institutional Official.

3 IRB Review Process

All human subjects research conducted under the auspices of BH is reviewed by one of the following methods:

- Exempt
- Expedited Review
- Facilitated Review (see Section 3.15.1 for a detailed discussion)
- Full Committee Review

The IRB will ensure that the research meets all required ethical and regulatory criteria for initial and continuing review and any modifications of approved research.

3.1 Definitions

Minimal Risk. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Minor Change. A minor change is one which, in the judgment of the IRB reviewer, makes no substantial alteration in:

1. the level of risks to subjects
2. the research design or methodology (adding procedures that are not eligible for expedited review would not be considered a minor change)
3. the number of subjects enrolled in the research (no greater than 10% of the total requested) unless the modification is to the local numbers in a multi-site study and the research is not Phase 1 or 2, Pilot, or Feasibility
4. the qualifications of the research team
5. the facilities available to support safe conduct of the research
6. Any other factor which would warrant review of the proposed changes by the convened IRB.

Quorum. A quorum of the IRB consists of a simple majority of the voting membership, including at least one member whose primary concern is in a non-scientific area. If research involving an FDA-regulated article is involved, a licensed physician must be included in the quorum.

Suspension of IRB approval. A suspension is a directive of the convened IRB or other authorized individual to temporarily stop some or all previously approved research activities. Suspended protocols remain open and require continuing review.

Termination of IRB approval. A termination of IRB approval is a directive of the convened IRB to stop permanently all activities in a previously approved research protocol. Terminated protocols are considered closed and no longer require continuing review.

3.2 Human Subjects Research Determination

The responsibility for initial determination as to whether an activity constitutes human subjects research rests with the investigator. The investigator should make this determination based on the definitions of “human subject” and “research” in Section 1.3. Since the institution will hold them responsible if the determination is not correct, investigators are urged to request a confirmation that an activity does not constitute human subjects research from the Human Research Protection Program. The request should be made by the prospective submission of an on-line request for a Human Subjects Research Determination via IRBNet. The HRPP is unable to provide a determination after an activity has taken place. All requests must include sufficient documentation of the activity to support the determination. Investigators are reminded that all research activity, whether human subjects or not, must be registered with the institution via IRBNet by submitting basic project information to Sponsored Programs Administration (SPA)

Determinations as to whether an activity constitutes human subjects research will be made according to the definitions in Section 1.3. Determinations regarding activities that are either clearly or clearly not human subjects research may be made by the HRPP Director or IRB Chair. Determinations regarding less clear-cut activities will be referred by the Director to the IRB Chair or designee, who may make the determination or refer the matter to the full IRB.

Submission materials and documentation of determinations will be recorded and maintained on IRBNet.

3.2.1 Research Utilizing Public Data Sets

Definitions:

Public Data Sets are publicly available data files prepared by investigators or data suppliers with the intent of making them available for public use.

Publicly Available means that the data are widely available. Data may still be considered publicly available when: (1) a fee is charged for obtaining the data, (2) access to the data is limited to researchers, if any researcher with a standard academic or research affiliation has access.

Restricted Use Data Sets are special files distributed by government agencies, research organizations, and others which have restrictions on access and use. These files may contain a subset of data specific to an institution which includes identifiers or when combined with institutional sources could lead to identification of individual subjects; or may contain direct identifiers such as names, medical record numbers, Social Security

Numbers, or addresses. Use restrictions apply such as specified data security standards and/or limited permissible analyses or uses.

Public data sets are a valuable resource for researchers. Most large public data sets are either de-identified in accordance with HIPAA or constitute a limited data set. Use of data from these data sets for research purposes does not constitute human subjects research under either the Common Rule or FDA regulations as: (1) the identity of the individual subject is not known and cannot be readily ascertained by the investigator, and (2) the research does not involve an experiment involving a FDA regulated test article and one or more human subjects.

Investigators who make use of these datasets for a research project do not need to submit for a human subjects determination and may rely on this policy for evidence of conformance with institutional policy if requested by a journal or data set holder. However the researcher must still “register” the research with the institution by submitting a core data form, protocol or research description, and a copy of any data use agreements via IRBNet to Sponsored Programs Administration.

When any of the following are true, this policy cannot be relied upon and a submission to the IRB is required:

1. The data host requires the researcher or the researcher’s institution to sign a Data Use Agreement that explicitly requires IRB approval, a human subjects determination, or a determination of exempt status.
2. The grantor requires IRB approval, a human subjects determination, or a determination of exempt status.
3. Restricted Use Data Sets or SubSets: Certain public data sets also have subsets of restricted use data which may contain data specific to an institution and/or more extensive identifiers.
4. The research includes data from other sources that may be considered identifiable under either HIPAA or the Common Rule.
5. The research will include merging of data sets in such a way that individuals may become identifiable.
6. The research includes other activities such as administration of surveys or focus groups which do meet the definition of human subjects research.
7. Any other circumstances where the research may meet the definition of human subjects research under the Common Rule or a clinical investigation per FDA regulations.

The following data sets have been reviewed by the Baystate HRPP and verified as meeting the requirements of a “Public Data Set”. The HRPP will review other data sets at the request of investigators and will add to this list as needed when policy revisions occur. Some of these data

sources also offer restricted use data, projects utilizing restricted use data require submission to the IRB.

1. American College of Surgeons National Trauma Data Bank (NTDB)
2. American Hospital Association Annual Survey
3. CDC Behavioral Risk Factor Surveillance System (BRFSS)
4. Healthcare Cost and Utilization Project (H-CUP) databases:
5. Nationwide Inpatient Sample (NIS)
6. Kids' Inpatient Database (KID)
7. Nationwide Emergency Department Sample (NEDS)
8. State Inpatient Databases (SID)
9. State Ambulatory Surgery Databases (SASD)
10. State Emergency Department Databases (SEDD)
11. Massachusetts Community Health Information Profile (MassCHIP)
12. Medicare Compare Databases:
13. Dialysis Facility Compare
14. Home Health Compare
15. Hospital Compare
16. Nursing Home Compare
17. Medicare Healthcare Cost Report Information System (HCRIS)
18. National Center for Health Statistics Public-Use Data Files
19. National Health and Nutrition Examination Survey (NHANES)
20. National Health Care Surveys (NCHS)
21. National Vital Statistics System (NVSS)
22. National Survey of Family Growth (NSFG)
23. National Health Interview Survey (NHIS)
24. National Immunization Survey (NIS)
25. Longitudinal Studies of Aging (LSOA)
26. State and Local Area Integrated Telephone Survey (SLAITS)
27. National Ambulatory Medical Care Survey (NAMCS)
28. National Hospital Ambulatory Medical Care Survey (NHAMCS)
29. National Survey of Children's Health, Public Use Data

30. Organ Procurement and Transplantation Network. Public Use Data

31. U.S. Census Bureau

32. U.S. Bureau of Labor Statistics

3.3 Exempt Studies

All research using human subjects must be approved by the Institution. Certain categories of research (i.e., “exempt research”) do not require convened IRB review and approval. Exempt research is subject to institutional review and must be determined and approved by the HRPP Director, IRB Chair, or designated IRB members.

3.3.1 Limitations on Research Subjects:

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

Prisoners: Exemptions do NOT apply. IRB review is required.

3.3.2 Categories of Exempt Research

With the above exceptions, research activities not regulated by the FDA in which the only involvement of human subjects will be in one or more of the following categories are exempt from IRB review, but require institutional review:

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

3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2), if:
 - a) the human subjects are elected or appointed public officials or candidates for public office; or
 - b) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

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

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

- b) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

3.3.3 FDA Exemptions

The following categories of clinical investigations are exempt from the requirements of IRB review:

1. Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review. [21 CFR 56.104(c)]

[Note: See Section 7.5 for detailed discussion of this exemption.]

2. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. [21 CFR 56.104(d)]

3.3.4 Procedures for Exemption Determination

In order to obtain an exemption determination investigators must submit:

1. an on-line application including a **Request for Determination of Exempt Status**;
2. all recruitment materials (e.g., letter of invitation, recruitment script, flyer),
3. consent form (when appropriate),
4. all surveys, questionnaires, instruments, etc.,
5. documentation of permission from each non-Baystate site of performance
6. if federally funded, one copy of the grant application(s) if Baystate is the primary awardee,
7. Verification of current human research protection training for all members of the research team.

The HRPP Director, IRB Chair, or designated IRB member reviews all requests for exemptions and determines whether the request meets the criteria for exempt research. The IRB Chair may

designate other IRB members to review requests for exemptions submitted to the IRB. The Chair selects designees who are qualified to review this category of submission based on their expertise and knowledge of regulations pertaining to research. Individuals involved in making the determination of exempt status cannot be involved in the proposed research and do not have any apparent conflict of interest.

To document the determination of the request for exempt research, the reviewer completes the worksheet for **Exemption Determinations**. The reviewer verifies whether the submission meets the criteria for exemption and indicates whether the request for exemption is approved, if modifications are required, or if the request is denied. If approved, the rationale for the determination and category under which it was permitted is documented. If denied, the rationale is documented and provided to the researcher.

Investigators will be notified as to the qualification of the application for exempt status by the IRB staff via IRBNet.

Exempt determinations are valid for a maximum of three years exemption with the date of expiration provided to the researcher in the exemption letter. If the research extends beyond that date then the researcher has to request another exemption. Investigators must complete a **Study Closure Report** when the research is complete.

3.3.5 Additional Protections

Although exempt research is not covered by the federal regulations, this research is not exempt from the ethical guidelines of the Belmont Report, HIPAA, and the policies of the institution and is subject to institutional oversight including HRPP compliance reviews. The individual making the determination of exemption will determine whether to require additional protections for subjects in keeping with the guidelines of the Belmont Report and institutional policies. The HRPP Director or IRB reviewer has the option to require that research technically exempt be subject to IRB review and oversight.

3.4 Expedited Review

An IRB may use the expedited review procedure to review the following:

- some or all of the research appearing on the list of categories of research eligible for expedited review and found by the reviewer(s) to involve no more than minimal risk,
- modifications to research previously determined to meet the criteria for expedited review if the allowable risk associated with the change is either no more than minimal risk or the risk-benefit relationship of the research is not altered in a way that makes it less favorable
- minor changes in previously approved research during the period (of one year or less) for which approval is authorized

3.4.1 Categories of Research Eligible for Expedited Review

The categories of research eligible for expedited review were published in a Federal Register Notice [63 FR 60364-60367, November 9, 1998].

The activities listed below should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

The categories in this list apply regardless of the age of subjects, except as noted.

The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

The expedited review procedure may not be used for classified research involving human subjects.

The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--utilized by the IRB.

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

(1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

(a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

(b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

(2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

(a) From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

(b) from other adults and children¹, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week. [¹Children are defined in the DHHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted."][[45 CFR 46.402\(a\)](#)]

(3) Prospective collection of biological specimens for research purposes by noninvasive means.

Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

OHRP has clarified its view about the meaning of "noninvasive." Under Expedited Review Category 3, the following procedures are also considered noninvasive:

- Vaginal swabs that do not go beyond the cervical os;
- Rectal swabs that do not go beyond the rectum; and
- Nasal swabs that do not go beyond the nares.

This clarification is consistent with the Food and Drug Administration's position on these procedures.

(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic

resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). [NOTE: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. See Exempt Categories and 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.]

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

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

(8) Continuing review of research previously approved by the convened IRB as follows:

(a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; *or*

(b) Where no subjects have been enrolled and no additional risks have been identified; *or*

(c) Where the remaining research activities are limited to data analysis.

[Of note, category (8) identifies three situations in which research that is greater than minimal risk and has been initially reviewed by a convened IRB may undergo subsequent continuing review by the expedited review procedure.

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

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

[Under Category (9), an expedited review procedure may be used for continuing review of research not conducted under an investigational new drug application or investigational device exemption where categories (2) through (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified. The determination that "no additional risks have been identified" does not need to be made by the convened IRB.]

3.4.2 Expedited Review Procedures

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

On an annual basis, the Chair will designate a list of IRB members eligible to conduct expedited review. The designees must be experienced (having served on the IRB for at least one year) members or alternate members of the IRB. The IRB Staff will select expedited reviewers from that list. Selected reviewers will have the qualifications, experience and knowledge in the content of the protocol to be reviewed, as well as be knowledgeable of the requirements to approve research under expedited review. IRB members with a conflict of interest in the research will not be selected.

When reviewing research under an expedited review procedure, the IRB Chair, or designated IRB member(s), has on-line access to the project file including the protocol, consent form if applicable, the application forms, and historical documents.

The reviewer conducting initial review completes the **Eligibility for Expedited Review** worksheet to determine whether the research meets the criteria allowing review using the expedited procedure and if so, completes the **New Submission** worksheet to determine whether the research meets the regulatory criteria for approval. If the research does not meet the criteria for expedited review, or if in the opinion of the reviewer should be reviewed by the convened IRB, then the reviewer will indicate that the research requires full review by the IRB and the protocol will be placed on the agenda for the next available IRB meeting.

The reviewer conducting continuing review determines whether the research meets the regulatory criteria for approval by using the **Continuing Review** worksheet and determines whether the submission meets the regulatory criteria for use of an expedited review procedure by using the Expedited Review Checklist contained within the worksheet.

In reviewing the research, the reviewers follow the Review Procedures described in Sections 3 and may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only when reviewed by the convened IRB.

Reviewers will indicate approval, required modifications or requirement for convened board review on the applicable worksheets. If modifications are required the IRB staff will inform the investigator via IRBNet. If the modifications are minor, the IRB Chair or designated IRB member may determine if the investigator has sufficiently addressed the modifications. If the modifications are major, or if the reviewer(s) request it, the modified protocol will be sent back to the initial reviewer for further review.

In the event that expedited review is carried out by more than one IRB member and the expedited reviewers disagree, the protocol will be forwarded to the convened IRB for review.

3.4.3 Informing the IRB

Members of the IRB are notified of all expedited review approvals via the agenda and minutes. Any non-conflicted IRB member can review the full protocol on-line upon request.

3.5 Convened IRB Meetings

Except when an expedited review procedure is used, the IRB will conduct initial and continuing reviews of all research at convened meetings at which a quorum (see below) of the members is present.

3.5.1 IRB Meeting Schedule

The IRB meets on a regular basis throughout the year (usually once per month). The schedule for the IRB may vary due to holidays or lack of quorum. The schedule for IRB meetings is found on the intranet. Special meetings may be called at anytime by the HRPP Director or the IRB Chair.

3.5.2 Preliminary Review

The IRB Analyst will conduct a preliminary review of all protocol materials submitted to the IRB for determination of completeness and accuracy. Only complete submissions will be placed on the IRB agenda for review. The investigator will be informed either by on-line communication, e-mail, phone, or in person of missing materials. In the case of a PI who is submitting a protocol for the first time or an investigator who may not be well-versed in the protocol submission procedures, individualized IRB consultations can be arranged. Specific questions about the HRPP policies and procedures, determination of whether a particular protocol is human research or not and what particular forms are required for a particular study can be submitted to the HRPP Director or any member of the HRPP or IRB staff for information and/or clarification. Individual appointments with the staff can also be arranged and are strongly recommended for first-time submissions.

All BH Investigator-initiated research will undergo a formal pre-review. Feedback will be provided to investigators on the content of the submission forms, the consent, and the protocol by the HRPP and IRB staff, and, as appropriate, the staff of the Epidemiological and Biostatistical Support Center.

3.5.3 Primary Reviewers

After it has been determined that the protocol submission is complete, the IRB Analyst, with the assistance of the HRPP Director or IRB Chair as needed, will assign protocols for review paying close attention to the scientific content of the protocol, the potential reviewer's area of expertise, and representation for vulnerable populations involved in the research. A primary reviewer is assigned to each submission for convened board review. A secondary reviewer may also be assigned at the discretion of the Director, Chair, or IRB Analyst. When the IRB is presented with a protocol which may be outside of the knowledge base or representative capacity of its members, an outside consultant will be sought. Protocols for which appropriate expertise cannot be obtained for a given meeting will be deferred to another meeting.

Primary reviewers are responsible for:

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

If a primary reviewer is to be absent from the meeting, a new reviewer may be assigned, providing the new reviewer has opportunity to review the materials prior to the meeting. Additionally, an absent reviewer can submit their written comments for presentation at the convened meeting, as long as there is another reviewer present at the convened meeting who can serve as the primary reviewer. It should be noted that all of the IRB members receive and are expected to review all studies, not just the ones they are assigned to as primary reviewer.

3.5.4 Pre-Meeting Distribution of Documents

All required materials must be submitted (in full) at least 10 business days prior to a convened meeting for possible inclusion on the following IRB agenda. In general, once approved, a protocol remains with the IRB that initially reviewed it. The HRPP Director may close an agenda to the addition of items at any time in order to provide adequate time at meetings for meaningful review and discussion. In addition, the HRPP Director and IRB staff have the discretion to assign items to a board based on the available expertise of the members. The

meeting agenda will be prepared by the IRB Analyst and distributed to the IRB members prior to the meeting. All IRB members receive their review materials which include the IRB agenda, applicable business items, appropriate continuing education materials, and protocol review materials no later than 5 business days before the scheduled meeting to allow sufficient time for the review process. On occasion, if a time sensitive item arises, it may be added on to the meeting agenda after these deadlines have passed. In these instances, the IRB members will be notified via email or phone call so that they are aware that an additional item requires their review.

3.5.5 Materials received by the IRB

Each IRB member receives and reviews the submission materials for all protocols on the agenda.

The primary reviewer must review: the grant application (if Baystate is the awardee institution); the sponsor's protocol (when one exists); the investigator's brochure (when one exists); the DHHS-approved sample consent document (when one exists); the complete DHHS-approved protocol (when one exists).

If an IRB member requires additional information to complete the review he or she may contact the investigator directly or ask the IRB Staff to make the request of the investigator.

IRB Members will utilize the applicable Reviewer Worksheets and the IRBNet "Reviewer Comments" tool to document their review and recommendations.

3.5.6 Quorum

A quorum consists of a simple majority (more than half) of the voting membership, including at least one member whose primary concern is in a non-scientific area. If research involving an FDA-regulated article is to be reviewed, a licensed physician must be included in the quorum. The IRB Chair, with the assistance of the IRB staff, will confirm that an appropriate quorum is present before calling the meeting to order. The IRB Chair will be responsible for ensuring that the meetings remain appropriately convened.

At meetings of the IRB, a quorum must be established and maintained for the deliberation and vote on all matters requiring a vote. The IRB staff takes note of arrivals and departures of all members and notifies the Chair if a quorum is not present. If a quorum is not maintained, the pending action item must be deferred or the meeting must be terminated.

Members are considered present if participating through teleconferencing or videoconferencing. In this case, the member must have received all pertinent material prior to the meeting and must be able to participate actively and equally in all discussions and votes.

Opinions of absent members transmitted by mail, telephone, facsimile or electronically may be considered by the attending IRB members but may not be counted as votes or to satisfy the quorum for convened meetings.

3.5.7 Meeting Procedures

The IRB Chair, or Vice-Chair or designee in the event that the IRB Chair is absent, will call the meeting to order, once it has been determined that a quorum is in place. The Chair will remind IRB members to recuse themselves from the discussion and vote by leaving the room when there is a conflict of interest. The IRB will review and discuss the IRB Minutes from the prior meeting and determine if there are any revisions/corrections to be made. If there are no changes to be made, the Minutes will be accepted as presented and considered final. If it is determined that revisions/corrections are necessary, the Minutes will be amended.

The IRB reviews all submissions for initial and continuing review, as well as requests for modifications. The Primary Reviewer presents an overview of the research proposal and leads the IRB through the completion of the regulatory criteria for approval utilizing the applicable worksheets. All members present at a convened meeting have full voting rights, except in the case of a conflict of interest or if both a member and their alternate are in attendance. In order for the research to be approved, it must receive the approval of a majority of those voting members present.

It is the responsibility of the IRB staff to record the proceedings of the session in order to later produce the meeting Minutes.

3.5.8 Guests

The Principal Investigator may attend the IRB meeting to answer questions about their proposed or ongoing research. The Principal Investigator may not be present for the final discussion or vote on their research.

Ex-officio guests are individuals who, by virtue of their position and their role in the HRPP, may attend IRB meetings. Ex-officio guests include the Institutional Official, the Research Integrity Officer, HRPP Integrity and Education Specialists, and the Director or staff of Sponsored Programs Administration. Ex-officio guests may participate in the IRB discussion and deliberations as long as they do not have a conflict of interest in the item being discussed. In the event of a conflict of interest, the ex-officio guest may answer questions if requested by the IRB, but leaves the meeting room for the final discussion and vote. Ex-officio guests may not vote.

Other guests may be permitted to attend IRB meetings at the discretion of the IRB Chair and/or the HRPP Director. Guests, other than ex-officio guests, may not speak unless requested by the IRB and must sign a confidentiality agreement.

3.6 Criteria for IRB Approval of Research

For the IRB to approve human subjects research, it must determine that the following requirements are satisfied:

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

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

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by §46.116.

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

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

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

(8) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

These criteria must be satisfied for each review (initial, continuing, and modifications) for both expedited review and review by the convened IRB.

3.6.1 Risk/Benefit Assessment

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

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

The assessment of the risks and benefits of proposed research involves a series of steps:

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

Risks to subjects are minimized:

1. by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk; and
2. Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

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

In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research - as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research.

The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

3.6.1.1 Scientific Merit

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

- the research uses procedures consistent with sound research design;

- the research design is sound enough to reasonably expect the research to answer its proposed question; and
- The knowledge expected to result from this research is sufficiently important to justify the risk.

In making this determination, the IRB may draw on its own knowledge and disciplinary expertise, or the IRB may draw on the knowledge and disciplinary expertise of others, such as reviews by a funding agency, or departmental review. When drawing on scientific review performed by an individual or entity external to the IRB, documentation of the review must be provided to the IRB.

At Baystate, departmental scientific review is documented by the electronic signature of the investigator's Department Chair or designee on new protocol applications or by the inclusion of a letter documenting the review in the submission package. Department specified requirements are detailed in the "Read Me First" document on IRBNet.

3.6.2 Selection of subjects is equitable.

The IRB determines by reviewing the application, protocol and other research materials that the selection of subjects is equitable with respect to gender, age, class, etc. The IRB will not approve a study that does not provide adequately for the equitable selection of subjects or has not provided an appropriate scientific and ethical justification for excluding classes of persons who might benefit from the research. In making this determination, the IRB evaluates: the purposes of the research; the setting in which the research occurs; scientific and ethical justification for including vulnerable populations such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons; the scientific and ethical justification for excluding classes of persons who might benefit from the research; and the inclusion/exclusion criteria.

At the time of the continuing review the IRB will assess whether or not the PI has followed the subject selection criteria that he/she/originally set forth at the time of the initial IRB review and approval.

3.6.2.1 Recruitment of Subjects

The investigator will provide the IRB with all recruiting materials to be used in identifying participants including recruitment methods, advertisements, and payment arrangements. See Section 3.7.

3.6.3 Informed Consent

The IRB will ensure that informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116 and 21 CFR 50.20. In addition, the IRB will ensure that informed consent will be

appropriately documented in accordance with, and to the extent required by 45 CFR 46.117 and 21 CFR 50.27. See Section 5 for detailed policies on informed consent.

3.6.4 Safety Monitoring

For all research that is more than minimal risk, the investigator must submit a safety monitoring plan. The initial plan submitted to the IRB should describe the procedures for safety monitoring, reporting of unanticipated problems involving risks to subjects or others, descriptions or interim safety reviews and the procedures planned for transmitting the results to the IRB. This description should include information regarding an independent Data and Safety Monitoring Board (DSMB), if one exists, or an explanation as to why an independent data safety monitor is not necessary.

The IRB determines that the safety monitoring plan makes adequate provision for monitoring the reactions of subjects and the collection of data to ensure the safety of subjects. The details of the monitoring plan may vary depending on the potential risks, complexity, and nature of the research study. The method and degree of monitoring is commensurate with the degree of risk involved. Monitoring may be conducted in various ways or by various individuals or groups, depending on the size and scope of the research effort. These exist on a continuum from monitoring by the principal investigator in a small, lower risk study to the establishment of an independent data and safety monitoring board for a large clinical trial.

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

1. Monitoring is commensurate with the nature, complexity, size and risk involved.
2. Monitoring is timely. Frequency should be commensurate with risk. Conclusions are reported to the IRB.
3. For lower risk studies, continuous, close monitoring by the study investigator or an independent individual may be an adequate and appropriate format for monitoring, with prompt reporting of problems to the IRB, sponsor and regulatory bodies as appropriate.
4. For an individual Safety Monitor the plan must include:
 - Parameters to be assessed
 - Mechanisms to assess the critical efficacy endpoints at intervals in order to determine when to continue, modify, or stop a study.
 - Frequency of monitoring
 - Procedures for reporting to the IRB

5. For a Data Safety Monitoring Board (DSMB), the plan must include:

- The name of the Data Safety Monitoring Board
- Where appropriate, the DSMB is independent from the sponsor
- Composition of the monitoring group (if a group is to be used): experts in all scientific disciplines needed to interpret the data and ensure patient safety. Clinical trial experts, biostatisticians, bioethicists, and clinicians knowledgeable about the disease and treatment under study should be part of the monitoring group or be available if warranted.
- Frequency, content, and availability of meeting reports
- The frequency and character of monitoring meetings (e.g., open or closed, public or private)
- Procedures for reporting to the IRB, Sponsor (when applicable), and regulatory bodies when appropriate

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

The IRB requires submission of Data and Safety Monitoring Board reports within 10 business days of receipt by the investigator or the research team or immediately if the report indicates that the health, safety or welfare of subjects is at risk.

3.6.5 Privacy and Confidentiality

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

3.6.5.1 Definitions

Privacy - having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.

Confidentiality - methods used to ensure that information obtained by researchers about their subjects is not improperly divulged.

Private information - information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

Identifiable information – information where the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

3.6.5.2 Privacy

The IRB must determine whether the activities in the research are appropriate in terms of privacy. In order to make that determination, the IRB must obtain information regarding how the investigators are getting access to subjects or subjects' private, identifiable information and the subjects' expectations of privacy in the situation. Investigators must have appropriate authorization to access the subjects or the subjects' information.

In developing strategies for the protection of subjects' privacy, consideration should be given to:

1. Methods used to identify and contact potential participants
2. Settings in which an individual will be interacting with an investigator
3. Appropriateness of personnel present for research activities
4. Methods used to obtain information about participants and the nature of the requested information
5. Information that is obtained about individuals other than the "target participants," and whether such individuals meet the regulatory definition of "human participant" (e.g., a subject provides information about a family member for a survey)
6. Limiting access to the minimum amount of information necessary to complete the study.

3.6.5.3 Confidentiality

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

The IRB ensures that the confidentiality of research subjects is protected. The IRB assesses whether there are adequate provisions to maintain confidentiality. The IRB does this through the evaluation of the methods used to obtain information:

- a. about subjects,
- b. about individuals who may be recruited to participate in studies,
- c. the use of personally identifiable records,
- d. and the methods to protect the confidentiality of research data.

The PI will provide the information regarding the confidentiality of research subjects at the time of initial review through the completion of the application, any necessary supplemental forms, research protocol, and/or other submitted, applicable materials. The IRB reviews the information received from the PI and determines whether or not the confidentiality of research subjects is sufficiently protected. In some cases, the IRB may also require that a Certificate of Confidentiality be obtained to additionally protect research data (See Section 17.1).

In reviewing confidentiality protections, the IRB shall consider the nature, probability, and magnitude of harms that would be likely to result from a disclosure of collected information outside the research. It shall evaluate the effectiveness of proposed de-identification techniques, coding systems, encryption methods, storage facilities, access limitations, and other relevant factors in determining the adequacy of confidentiality protections. The IRB may rely on an analysis by BH Information Security in assessing the adequacy of electronic protections.

3.6.6 Vulnerable Populations

At the time of initial review the IRB will consider the scientific and ethical reasons for including vulnerable subjects in research. The IRB may determine and require that, when appropriate, additional safeguards are put into place for vulnerable subjects, such as those with impaired decision-making capacity.

For an extensive discussion about the IRB's review and approval process for individual populations of vulnerable subjects, please refer to Section 6.

3.7 Additional Considerations during IRB Review and Approval of Research

3.7.1 Determination of Risk

At the time of initial and continuing review, the IRB will make a determination regarding the risks associated with the research protocols. Risks associated with the research will be classified as either "minimal" or "greater than minimal". This determination may change over time as the requirements of the research change. The meeting minutes will reflect the Committee's determination regarding risk levels.

3.7.2 Period of Approval

At the time of initial review and at continuing review, the IRB will make a determination regarding the frequency of review of the research protocols. All protocols will be reviewed by the IRB at intervals appropriate to the degree of risk but no less than once per year. In some circumstances, a shorter review interval (e.g. semi-annually, quarterly, or after accrual of a specific number of participants) may be required (see below). The meeting minutes will reflect the IRB's determination regarding review frequency.

3.7.2.1 Review More Often Than Annually

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

1. Significant risk to research subjects (e.g., death, permanent or long lasting disability or morbidity, severe toxicity) without the possibility of direct benefit to the subjects;
2. The inclusion of especially vulnerable populations likely to be subject to coercion
3. A history of serious or continuing non-compliance on the part of the PI.

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

1. The probability and magnitude of anticipated risks to subjects.
2. The likely medical condition of the proposed subjects.
3. The overall qualifications of the PI and other members of the research team.
4. The specific experience of the PI and other members of the research team in conducting similar research.
5. The nature and frequency of adverse events observed in similar research at this and other institutions.
6. The novelty of the research making unanticipated adverse events more likely.
7. Any other factors that the IRB deems relevant.

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

enrolled in less than 1 year. If an approval period of less than one year is specified by the IRB the reason for more frequent review is documented in the minutes.

3.7.3 Independent Verification That No Material Changes Have Occurred

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

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

1. Protocols where concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources.
2. Protocols conducted by Principal Investigators who have previously failed to comply with federal regulations and/or the requirements or determinations of the IRB.
3. Protocols randomly selected for internal review.
4. Whenever else the IRB deems verification from outside sources is relevant.

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

1. The probability and magnitude of anticipated risks to subjects.
2. The likely medical condition of the proposed subjects.
3. The probable nature and frequency of changes that may ordinarily be expected in the type of research proposed.

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

If material changes have occurred without IRB review and approval, the IRB will determine the corrective actions to be taken.

3.7.4 Consent Monitoring

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

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

See Section 5.7 for a detailed discussion of consent monitoring.

3.7.5 Investigator Conflicts of Interest

The Principal Investigator and each member of the research team must complete and submit a **Conflict of Interest/Commitment Questionnaire** at initial and continuing review. IRB staff will review these forms to identify potential conflict of interests(COI) and forward those studies with a potential COI to the Research Integrity Officer (RIO) who will review the disclosures and the study and obtain further information from available sources, as the RIO deems necessary. The RIO may convene a meeting of the Research COI Committee. The RIO will serve as Chair of the Research COI Committee. The Research COI Committee will consider all information collected by the RIO and may request further information be obtained. The RIO will make a report to the IRB which includes a summary of the facts, a conclusion as to whether or not an actual or potential conflict exists, and may include recommendations for addressing the circumstances, which may include management and/or disclosure of the conflict.

The IRB will review the report and recommendations of the RIO and/or Research COI Committee and make a final determination as to whether a conflict of interest exists with regard to the research under review and the actions to take in regards to management and/or disclosure. If disclosure to potential subjects is required, the IRB will determine the form, detail, and extent of the required disclosure. If a conflict of interest exists, final IRB approval cannot be given until an approved conflict management plan is in place or determined to be unnecessary.

In reviewing conflicts and proposed management plans, the IRB considers all of the facts and circumstances including such factors as:

1. Whether the conflict, financial or non-financial, affects the protections of research participants,
2. Whether a competing interest could create an actual conflict of interest or the appearance of a conflict of interest for the investigator, the IRB or one of its members, or the HRPP.
3. How the research is supported or financed,

4. By whom the study is designed,
5. The ability of the conflicted individual, given the study design, to influence the data, results, or outcome of the study.

A conflict management plan may include conditions such as the following:

1. Disclosure to subjects through the consent process
2. Modification of the research protocol or safety monitoring plan
3. Monitoring of research by independent reviewers
4. Disqualification of the conflicted party from participation in all or a portion of the research
5. Appointment of a non-conflicted Principal Investigator
6. Divestiture of significant financial interests
7. Severance of relationships that create actual or potential conflicts
8. Prohibition of the conduct of the research at the institution

For a detailed discussion of Conflict of Interest see [AA Policy BH-AA-2.02](#).

3.7.6 Significant New Findings

During the course of research, significant new knowledge or findings about the medication, test article, and/or the condition under study may develop. The PI must report any significant new findings to the IRB and the IRB will review them with regard to the impact on the subjects' rights and welfare. Since the new knowledge or findings may affect the risks or benefits to subjects or subjects' willingness to continue in the research, the IRB may require that the PI contact the currently enrolled subjects to inform them of the new information. The IRB will communicate this to the PI. The IRB may require that the consent document be updated and that the currently enrolled subjects be re-consented, acknowledging receipt of this new information and for affirming their continued participation. Alternatively, the IRB may require that an information sheet or letter be provided to participants and that this is documented. The content of such letters or information sheets must be reviewed and approved by the IRB prior to distribution unless necessary to eliminate apparent immediate hazards to the subject in which case the IRB must be promptly informed.

3.7.7 Advertisements

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

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

This information should be submitted to the IRB with the initial application or as a modification (amendment) to the protocol.

The IRB reviews the material to assure that the material is accurate and is not coercive or unduly optimistic, creating undue influence to the subject to participate which includes but is not limited to:

1. Statements implying a certainty of favorable outcome or other benefits beyond what was outlined in the consent document and the protocol.
2. Claims, either explicitly or implicitly, that the drug, biologic or device was safe or effective for the purposes under investigation
3. Claims, either explicitly or implicitly, that the test article was known to be equivalent or superior to any other drug, biologic or device
4. Using terms like “new treatment,” “new medication,” or “new drug” without explaining that the test article was investigational
5. Promising “free medical treatment” when the intent was only to say participants will not be charged for taking part in the investigation
6. Emphasis on payment or the amount to be paid, such as bold type or larger font on printed media
7. Promise of “coupons” good for a discount on the purchase price of the product once it has been approved for marketing
8. The inclusion of exculpatory language.

Any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest. When appropriately worded, the following items may be included:

1. The name and address of the clinical investigator and/or research facility.
2. The condition being studied and/or the purpose of the research.
3. In summary form, the criteria that will be used to determine eligibility for the study.

4. The time or other commitment required of the subjects.
5. The location of the research and the person or office to contact for further information.
6. A clear statement that this is research and not treatment.
7. A brief list of potential benefits (e.g. no cost of health exam).

It is the policy of BH that all such materials also be reviewed and approved by Marketing and Communications. The Principal Investigator is responsible for securing and documenting this approval.

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

Directory listings of research such as ClinicalTrials.Gov are not considered advertisements and therefore do not require IRB review and approval if the listing is limited to the following basic trial information: title, purpose of the study, protocol summary, basic eligibility criteria, study site location(s), and how to contact the study site for further information.

3.7.8 ResearchMatch – The National Recruitment Registry

The ResearchMatch registry is available to Baystate investigators as a recruitment tool for research. The investigator is responsible for accessing and using the [ResearchMatch website](#) in accordance with the Researchers Acknowledgement Form (available on eWorkplace and in IRBNet), and all applicable Baystate Health policies and procedures. ResearchMatch should be identified as an advertisement and recruitment tool on the appropriate IRB application forms. IRB approval of ResearchMatch as a recruitment tool is required prior to submitting requests to ResearchMatch.

3.7.9 Payment to Research Subjects

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

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

- a) Substantiate that proposed payments are reasonable and commensurate with the expected contributions of the subject;

b) State the terms of the subject participation agreement and the amount of payment in the informed consent form; and

c). Substantiate that subject payments are fair and appropriate, and that they do not constitute (or appear to constitute) undue pressure on the potential participant to volunteer for the research study.

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

Credit for payment should accrue and not be contingent upon the participant completing the entire study. The IRB does not allow the entire payment to be contingent upon completion of the entire study. Any amount paid as bonus for completion of the entire study should not be so great that it becomes coercive.

The consent form must describe the terms of payment and the conditions under which subjects would receive partial payment or no payment (e.g., if they withdraw from the study before their participation is completed).

The BH Offices of Accounts Payable and Cashier Services require identifying information to issue checks, cash, or gift certificates to subjects. The consent form must inform subjects that they will be asked to provide identifying information including their Social Security Number to receive payment and that payments may be reportable to the IRS.

3.7.10 Raffles and Games of Chance in Research Studies

Massachusetts law controls the use and conduct of raffles and other games of chance. A raffle is a form of gambling and careful consideration should be given to the relative risk of encouraging negative behaviors. BH HRPP permits the use of a raffle only in very limited circumstances.

A raffle or any other game of chance may be used in a research protocol only if all of the following conditions are met:

1. the use of a raffle or game of chance must be justified as necessary to advance the goal of the research, appropriate for the subject population, and designed to minimize the risk of encouraging negative behaviors.
2. all research subjects are: (a) BH employees; (b) BH residents; (c) on the medical staff or associate professional staff of a BH facility; or (d) students doing a clinical rotation at a BH facility if a faculty member of the student's educational institution has given permission.
3. The criteria for entering the raffle must be clear to all potential subjects and all persons who meet the criteria must be permitted to enter the raffle.

4. The prize is a modest, non-cash item. Gift cards \$25 or less are permitted. Items with a fair market value of up to \$150 are permitted.
5. The raffle is used as a one-time incentive to participate in the research study and must not be integral to the protocol. For example, entry into a raffle to complete a survey is permissible; entry into a raffle on a weekly basis to incentivize compliance in a behavior modification protocol is not permissible.

No other use of a raffle or any other game of chance is permitted.

Contact the HRPP Director for further guidance.

3.7.11 Payments to Baystate or Investigators

Payment arrangements must avoid components that could influence or appear to influence how patients are enrolled. Payment terms must adhere to these principles:

1. Payments must be based on the costs of providing all components necessary to conduct the research, including personnel, and reflect fair market value.
2. Per-subject payments are generally acceptable if the payment is based on actual costs and is the same throughout the life of the trial, or if payments are made to fixed milestones.
3. A per-subject payment schedule that increases after a certain number of subjects are enrolled is not acceptable unless associated with actual increases in costs.
4. Payment that is provided only if a specified number of subjects are enrolled is not acceptable.
5. Bonus payments tied to the rate, timing, or number of subjects enrolled are not acceptable.
6. Any type of incentive, monetary or non-monetary, to refer or enroll subjects, so-called “finder’s fees,” are strictly prohibited.

3.7.12 Compliance with all Applicable State and Local Laws

The IRB adheres to all applicable state and local laws in the jurisdictions where the research is taking place. The HRPP and the IRB rely on an attorney for the interpretations and applications of Massachusetts law and the laws of any other jurisdiction where research is conducted as they apply to human subjects research. The IO arranges for appropriate legal counsel. Legal counsel may consist of BH staff or outside counsel.

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

3.8 Possible IRB Actions

3.8.1 Actions When Research Undergoes Review by the Convened Board

Approval - the study is approved as submitted.

Modifications Required - the protocol, consent, or other application materials require specific revisions, confirmation of IRB assumptions or understandings of how the research will be conducted is necessary, or additional documents are required to achieve approval.

Requirements are agreed upon at the meeting and are presented to the Principal Investigator via an IRB review letter for incorporation by simple concurrence or conformance. Note: The IRB cannot approve research that does not meet the criteria stipulated in the regulations. If the convened IRB cannot judge whether the criteria are met or believe that the criteria are not met then it cannot approve the research with conditions. This means that when the convened IRB approves research as Modifications Required, the conditions are prescriptive in nature.

In order to receive approval for a protocol designated “Modifications Required” by the convened board:

- The investigator’s response and any new or revised study documents are given to the IRB Chair, Vice Chair, or a designated member of the IRB for review. The reviewer(s) may approve the study upon receipt and approval of the revisions without further action by the IRB as long as the requirements of the board have been satisfied. If the contingencies of approval are unable to be satisfied or if the investigator proposes an alternative solution, the response to the IRB must be returned to the convened board for review.

Approval of the research will not be granted until all deficiencies are corrected to the satisfaction of the IRB or the reviewer(s).

The outcome of the IRB's deliberations is once again communicated to the investigator in writing.

The IRB's determination concerning the subsequent response to the IRB will be documented in the IRB minutes in the sections for expedited review.

[Note: For full review, the expiration date for the protocol is calculated based on the date that convened IRB reviewed the protocol and NOT on the final approval date.]

Deferred - This action is taken if substantial modification or clarification is required where the response may necessitate reconsideration of the criteria for approval, or insufficient information is provided to judge the protocol application adequately (e.g., the risks and benefits cannot be assessed with the information provided). IRB approval of the proposed research must not occur until subsequent review of the material the PI submitted by the convened IRB.

In order to receive approval for a deferred protocol:

- The investigator's response must be submitted for review at a subsequent, convened meeting of the same IRB. The IRB Office provides the IRB with the investigator's response and any new or revised study documents. The item is placed on the agenda for review at the next available meeting.

Approval of the protocol application will not be granted and certification will not be issued until all deficiencies, if any, are corrected to the satisfaction of the IRB.

The outcome of the IRB's deliberations is once again communicated to the investigator in writing.

The IRB's determination concerning the subsequent amended submission will be documented in the agenda and minutes .

Tabled – The primary reviewer was unable to attend the IRB meeting, the required constitution of board members was not present, or quorum otherwise failed. In this instance, the members of the board present may choose to table the item and provide informal feedback or recommendations, but not requirements, to the investigator.

Disapproved - The IRB has determined that the research cannot be conducted at BH or by employees or agents of BH or otherwise under the auspices of BH.

3.8.2 IRB Actions When Research Undergoes Expedited Review

Approval - the study is approved as submitted.

Modifications Required - the protocol, consent, or other application materials require revision, clarification or confirmation is necessary, or additional documents are required to achieve approval. Requirements and questions are presented to the Principal Investigator via an IRB review letter for incorporation by simple concurrence or conformance.

In order to receive approval for a protocol designated "Modifications Required":

- The investigator's response and any new or revised study documents are given to the same reviewer(s) for re-review whenever possible; otherwise, review is done by the IRB Chair or designee.

Approval of the protocol application will not be granted until all deficiencies are corrected to the satisfaction of the reviewer(s).

The outcome of the IRB's deliberations is once again communicated to the investigator in writing.

The IRB's determination will be documented in the IRB minutes in the sections for expedited review.

[Note: For expedited review, the expiration date for the protocol is calculated based on the final approval date.]

Information Required – the IRB reviewer has a question or is requesting clarification but no revisions to study documentation are required at this time. The question(s) or request for clarification are presented to the Principal Investigator via an IRB review letter.

In order to receive approval for a protocol designated “Information Required”:

- The investigator’s response and any new or revised study documents are given to the same reviewer(s) for re-review whenever possible; otherwise, review is done by the IRB Chair or designee.

Approval of the protocol application will not be granted until all deficiencies are corrected to the satisfaction of the reviewer(s).

The outcome of the IRB's deliberations is once again communicated to the investigator in writing.

The IRB's determination will be documented in the IRB minutes in the sections for expedited review.

[Note: For expedited review, the expiration date for the protocol is calculated based on the final approval date.]

Referral to the Full Board – the expedited reviewer finds that the research is not eligible for expedited review or believes convened board review or discussion is warranted. The item is placed on the agenda for the next available board meeting. Note: Research cannot be disapproved by expedited review, when an expedited reviewer believes that the criteria for approval cannot be satisfied the research must be referred to the convened board for review.

3.8.3 Approval in Principle

As per federal regulations, (45CFR46.118), there are two circumstances in which the IRB may grant approval required by a sponsoring agency without having reviewed all of the study procedures and consent documents. One is if study procedures are to be developed during the course of the research, but human subjects approval is required by the sponsoring agency. The other is if the involvement of human subjects depends on the outcomes of work with animal subjects. The IRB may then grant approval without having reviewed the as yet undeveloped recruitment, consent, and intervention materials. However, if the proposal is funded, the Principal Investigator must submit such materials for approval at least 60 days before recruiting human subjects into the study, or into any pilot studies or pre-tests. Approval in principle is granted to satisfy sponsoring agency requirements or to allow investigators to have access to funding to begin aspects of the project that do not involve human subjects.

3.9 Study Suspension, Termination and Investigator Hold

3.9.1 Suspension/Termination

IRB approval may be suspended or terminated if research is not being conducted in accordance with IRB or regulatory requirements or has been associated with unexpected problems or serious harm to subjects. (See Section 8 for a discussion of unexpected problems and Section 11 for a discussion of non-compliance)

Suspension of IRB approval is a directive of the convened IRB or IRB Chair either to temporarily stop some or all previously approved research activities short of permanently stopping all previously approved research activities. Suspended protocols remain open and require continuing review.

Termination of IRB approval is a directive of the convened IRB to stop permanently all activities in a previously approved research protocol. Terminated protocols are considered closed and no longer require continuing review. Terminations of protocols approved under expedited review must be made by the convened IRB.

The IRB shall notify the PI in writing of suspensions or terminations and shall include a statement of the reasons for the IRB's actions. The terms and conditions of the suspension must be explicit. The investigator can request the IRB reconsider a suspension or termination as described in Section 13.4.

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

The Institutional Official may suspend or terminate institutional approval of research. The suspension or termination of institutional approval will be reported to the IRB; and, in the case of termination, the IRB staff will administratively close the protocol.

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

If follow-up of subjects for safety reasons is permitted or required by the IRB or individual ordering the suspension or termination, the IRB or individual ordering the suspension or

termination may require that the subjects should be so informed and that any problems or adverse outcomes be reported to the IRB and the sponsor.

Investigators MUST continue to provide reports on unanticipated problems and other events to both the IRB and sponsor just as if there had never been a suspension (i.e., all events that need to be reported during a study need to continue to be reported during the suspension period.)

3.9.2 Investigator Hold

An investigator may request a hold on a protocol when the investigator wishes to temporarily or permanently stop some or all approved research activities. An investigator hold is initiated by an investigator. Investigator holds are not suspensions or terminations.

3.9.2.1 Procedures

1. Investigators must notify the IRB in writing of the following:
 - a. That they are voluntarily placing a study on hold
 - b. A description of the research activities that will be stopped
 - c. Proposed actions to be taken to protect current participants
 - d. Any actions that will be taken prior to IRB approval of proposed changes in order to eliminate apparent immediate harm
2. Upon notification by the investigator of the hold the IRB Analyst places the research on the agenda for review and notifies the HRPP Director and IRB Chair.
3. The HRPP Director and the IRB Chair, in consultation with the investigators, determines whether any additional procedures need to be followed to protect the rights and welfare of current participants as described in “Protection of currently enrolled participants” below.
4. The HRPP Director and the IRB Chair, in consultation with the investigators, determines if, how, and when currently enrolled participants will be notified of the hold.
5. Investigators must request approval to restart research that has been subject to an investigator hold by submitting a modification request to the IRB. If the lifting of the hold does not change the research or if the changes are minor changes that do not impact risk, the modification can be reviewed and approved by expedited review. If the lifting of the investigator hold is associated with more than minor changes in the research, the modification must be reviewed by the convened IRB.

3.9.3 Protection of Currently Enrolled Participants

Before an investigator hold, termination, or suspension, is put into effect the convened IRB or IRB designee considers whether any additional procedures need to be followed to protect the rights and welfare of current participants. Such procedures might include:

- Transferring participants to another investigator
- Making arrangements for clinical care outside the research
- Allowing continuation of some research activities under the supervision of an independent monitor
- Requiring or permitting follow-up of participants for safety reasons
- Requiring adverse events or outcomes to be reported to the IRB and the sponsor
- Notification of current participants
- Notification of former participants

3.10 Continuing Review

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

For multicenter trials, continuing review is no longer required once all local data has been submitted and no research activity or data analysis is ongoing locally.

3.10.1 Approval Period

At Baystate, determination of the approval period and the need for additional supervision is made by the IRB on a protocol-by-protocol basis. For example, for particularly risky research, or for an investigator who has recently had a protocol suspended by the IRB due to regulatory concerns, an on-site review by the Integrity and Education Specialist or a subcommittee of the IRB might occur, or continuing review might be required before one year or after enrollment of the first several subjects.

For each initial or continuing approval the IRB will determine the approval period and specify the expiration date. IRB approval is considered to have lapsed at midnight on the expiration date of the approval. For a study approved by the convened IRB, the approval period starts on the date that the IRB conducts its final review of the study; that is, the date that the convened

IRB approved the research or the date the convened IRB required modifications to the research for non-substantive issues. For a study approved under expedited review, the approval period begins on the date the IRB Chair or IRB member(s) designated by the Chair gives final approval to the protocol.

The approval date and expiration date are clearly noted on IRB approval letters and must be strictly adhered to. Investigators must allow sufficient time for development and review of Continuing Review submissions. Continuing Review Reports must be submitted a minimum of 60 days prior to expiration in order to allow sufficient time for modifications and re-review if necessary by the IRB.

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

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

3.10.2 Continuing Review Process

To assist investigators IRBNet will send out renewal alerts to investigators 90 days, 75 days, 60 days, and 45 days in advance of the expiration date; however, it is the investigator's responsibility to ensure that the continuing review of ongoing research is approved prior to the expiration date. By federal regulation, no extension to that date can be granted.

Investigators must submit the following for continuing review:

1. Continuing Review Report
2. Publication(s) related to the research
3. Any un-submitted reports identified while completing the continuing review report*
4. Conflict of Interest and Commitment Questionnaire for each member of the research team

The study's historical documents are accessible to the IRB reviewer on IRBNet.

In conducting continuing review of research not eligible for expedited review, all IRB members are provided with on-line access to the above and the project history. The Primary Reviewer will review all of the above and the complete protocol, including any modifications previously approved by the IRB. At the meeting, the Primary Reviewer leads the IRB through the completion of the regulatory criteria for approval in the **Continuing Review** worksheet.

IRB staff attend the convened meetings and bring a laptop to allow access to the protocol files for each protocol on the agenda. The IRB staff will retrieve any additional related materials the IRB members request.

In the case of expedited review, the IRB members have full access to the submission documents on IRBNet.

Review of currently approved or newly proposed consent documents must occur during the scheduled continuing review of research by the IRB, but **consent documents should be reviewed whenever new information becomes available** that would require modification of information in the consent document.

3.10.3 Expedited Review of Continuing Review

In conducting continuing review under expedited review, the reviewers receive all of the above material. The reviewer(s) complete the **Continuing Review Report** to determine whether the research meets the criteria allowing continuing review using the expedited procedure, and if so, whether the research continues to meet the regulatory criteria for approval.

Generally, if research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, except in limited circumstances described by expedited review categories (8) and (9) at 63 FR 60364-60367 (see Expedited Review Categories). It is also possible that research activities that previously qualified for expedited review in accordance with 45 CFR 46.110, have changed or will change, such that expedited IRB review would no longer be permitted for continuing review.

3.10.4 Management of a Lapse in Continuing Review

The regulations permit no grace period or approval extension after approval expiration. Research that continues after the approval period has expired is research conducted without IRB approval. If the continuing review does not occur prior to the expiration as specified by the IRB, all research activities must stop, including recruitment (media advertisements must be pulled), enrollment, consent, interventions, interactions, and data collection, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. This will occur even if the investigator has provided the continuing information before the expiration date. Therefore, investigators must allow sufficient time for IRB review before the expiration date.

IRBNet sends an “Expiration Notice” alert to notify investigators of lapses in IRB approval and to advise the investigator that all research activities must stop until approval to continue is received.

If research participants are currently enrolled in the research project and their participation is ongoing, once notified of the expiration of approval the PI must immediately submit to the IRB Chair or designee a list of research subjects for whom suspension of the research would cause

harm and an explanation as to why harm would occur. Enrollment of new subjects cannot occur and continuation of research interventions or interactions for already enrolled subjects may only continue when the IRB or IRB Chair or designee concludes that it is in the best interest of the individual subjects to do so.

Failure to submit continuing review information on time is non-compliance and will be handled according to the non-compliance policy (See Section 11).

Once approval has expired, IRB review and re-approval must occur prior to re-initiation of the research. If the study approval has lapsed more than 45 days and the PI has not provided the required continuing review information, the PI must submit a new application to the IRB for review and approval. If the study approval has lapsed 45 days or less and the PI provides the required continuing review information, the existing protocol may be reviewed for consideration of continued IRB approval. Exceptions to the 45 day stipulation may be approved on a case by case basis by the IRB Chair or Director.

If modifications are required by the IRB at the time of the continuing review and the approval expires before the PI responds to the requirements, all research activities must stop and the procedures described above for existing subjects must be followed. Once the PI responds, the existing protocol will be reviewed for continuation. If the PI does not respond for an extended period, the IRB may administratively close the study. Decisions of this kind must be made in a manner that ensures that closure will not harm any participants previously enrolled who may require ongoing treatment as part of the research study.

3.11 Amendment of an Approved Protocol

Investigators may wish to modify or amend their approved applications. **Investigators must seek IRB approval before making any changes in approved research** unless the change is necessary to eliminate an immediate hazard to the subject (in which case the IRB must then be notified at once).

Modifications may be approved if they are within the scope of what the IRB originally authorized. For example, if a researcher wishes to add a population to an existing study, but not alter the study procedures or purpose, a modification request is usually appropriate. Likewise, modifying a procedure without changing the study's purpose or study population may also be appropriate. If, however, the researcher wishes to modify the research in such a manner as it is no longer consistent with the scope or intent of the original project, he or she will need to submit a new application for human subjects approval.

Investigators must submit documentation to inform the IRB about the proposed changes to the research, including, but necessarily limited to:

- Completed “**Modification Request**” form;
- Revised Core Data Form, Basic Application Part 1, Basic Application Part 2 if applicable

- Revised protocol (if applicable)
- Revised consent/parental permission/assent documents (if applicable) or other documentation that would be provided to subjects when such information might relate to their willingness to continue to participate in the study
- Revised or additional recruitment materials
- Any other relevant documents provided by the sponsor or investigator

The IRB should be provided with revisions to documents with a “tracked changes” version and a “clean copy”. For sponsored protocols, a detailed summary of changes as provided by the sponsor is acceptable.

IRB staff will conduct an initial assessment to determine whether the proposed changes may be approved through an expedited review process or whether the modification warrants full board review. The reviewer(s) using the expedited procedure has the ultimate responsibility to determine that the proposed changes may be approved through the expedited review procedure and, if not, must refer the protocol for full board review.

3.11.1 Expedited Review of Protocol Modifications

An IRB may use expedited review procedures to review minor changes in ongoing previously-approved research during the period for which approval is authorized. An expedited review may be carried out by the IRB Chair and/or designated IRB members.

The reviewer(s) complete the **Modification Request** worksheet to determine whether the modifications meet the criteria allowing expedited review of the amendment, and if so, whether the research with the proposed modifications continues to meet the regulatory criteria for approval.

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

3.11.2 Full Board Review of Protocol Modifications

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

All IRB members are provided and review the documents provided by the investigator.

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

When the IRB reviews modifications to previously approved research, the IRB considers whether information about those modifications might relate to participants' willingness to continue to take part in the research and if so, whether to provide that information to participants.

3.12 Closure of Protocols

The completion or termination of the study, whether premature or not, is a change in activity and must be reported to the IRB. Investigators submit closure applications to the IRB as a **Study Closure Report**.

IRB staff review closure applications for completeness. Closure applications are reviewed and approved by the IRB Chair or designated IRB member(s). Notifications of closures are included on the IRB agenda.

3.13 Reporting IRB Actions

All IRB actions are communicated to the Principal Investigator (PI), or designated primary contact person for the protocol, in writing on-line typically within five working days via a template letter prepared by the IRB staff. For an approval, if applicable, a copy of the approved consent form containing the stamp of the IRB with the dates of the approval and expiration will also be provided to the investigator. For a "modifications required" or a deferral notice, the notification will include the modifications required for approval along with the basis for requiring those modifications. For a disapproval, termination, or suspension, the notification will include the basis for the decision.

All correspondence to investigators will be maintained in the electronic protocol file.

The IRB reports its findings and actions to the institution in the form of its minutes, which are distributed by IRB staff to the Institutional Official and are stored permanently and securely in the IRB Office for 2 years after which they are archived in a secure records storage facility.

3.14 Appeal of IRB Decisions

When an IRB protocol presented at a convened meeting is disapproved, deferred or requires minor modifications, the IRB will notify the PI in writing about the specific deficiencies and the modifications that are necessary for IRB approval. The IRB shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in writing.

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

Since the IO is responsible for policies and procedures followed by the IRB, the IO may review IRB decisions to ensure that the decision-making process is appropriate. If the IO has concerns regarding the process that the IRB has followed in making a decision, he/she may require the IRB to reconsider the decision. However, the IO cannot overrule an IRB decision.

3.15 Off-site IRB Policies and Procedures

3.15.1 National Cancer Institute's Central IRB

BH is a participant in the National Cancer Institute's Central Institutional Review Board (CIRB) Initiative for Radiation Therapy Oncology Group (RTOG) studies only. Local investigators who wish to enroll patients onto CIRB-approved protocols are encouraged to utilize this service. Such investigators should first contact the IRB office so that a username and password for the PI and study coordinator may be requested from the CIRB. NCI requires that investigators wishing to use a CIRB must first submit CIRB review materials and locally required materials to the on-site IRB for a facilitated review by one member, who will review the acceptability of CIRB as the IRB of record for that particular study.

Investigators wishing to utilize the NCI CIRB must:

1. Submit an on-line application to the on-site IRB that contains:
 - The Core Data Form and IRB Basic Applications Part 1 and 2 and any identified supplemental forms including the supplement for CIRB Facilitated Review
 - The electronic signatures of any applicable ancillary services or committees.
 - The CIRB documents identified on the Facilitated Review form.
 - The CIRB-approved consent form, modified as follows:
 - Apply local boilerplate requirements to the consent document including HIPAA section, contact information or any other information to comply with state or local laws, our institutional requirements or IRB policies.
 - Make minor word substitutions or additions in the consent document to facilitate better comprehension by the local populations as long as the proposed changes do not alter the meaning of the CIRB-approved contents

- Revisions/changes to the consent documents other than those described above require local review by the Convened Board, and facilitated review may not be used.
2. Designated IRB member(s) will conduct a facilitated review. There are three possible outcomes, relayed to the PI via IRBNet:
- **Approved (for CIRB Oversight):** The CIRB will be designated as the IRB of record. You will receive an acceptance letter, a copy of the confirmation e-mail from the CIRB, and a copy of the local consent document(s).
 - **Modifications Required (in order to secure approval for CIRB Oversight):** Specific stipulations must be addressed before the CIRB can be designated as the IRB of record.
 - **Deferred: Protocol Not Accepted (for CIRB Oversight):** Local IRB oversight is required. You must complete a local IRB application and submit materials to the IRB office via the standard application process. The CIRB will not be permitted to oversee the protocol.

When a Protocol has been Approved for CIRB Oversight

1. Designated staff notifies CIRB (via their website) and the PI (via IRBNet). Stamped consent documents are provided for use by PI and study team.
2. Once the CIRB is designated as the IRB of record for a study, PI's interaction with the HRPP Office and the IRB includes:
 - **Consent Form Revisions by CIRB:** PI must make all changes on the local consent/permission/assent form, update the header to match the CIRB approved consent and submit to the IRB for review.
 - **Continuing Reviews:** Continuing review will be conducted by the CIRB. All applicable CIRB paperwork should be submitted to the HRPP Office, along with a copy of CIRB's review for the study, the updated local consent form, and the BMC IRB Continuing Review Report. Materials will be reviewed by the IRB Chair or designee. Notification regarding review outcome (approval, modifications required etc) will be sent to PI. If approved, consent forms will receive updated stamping.

- Local Unanticipated Problems, Protocol Deviations, and all other local reporting requirements must be adhered to.
- Any local personnel changes, local advertisements, etc. must be submitted to the IRB for review and approval. Notification regarding review outcome (approval, modifications required, etc) will be sent to PI.
- Study Closure: To close a CIRB study at this site, PI submits a **Study Closure Report** to the IRB, who will, in turn, notify the CIRB as necessary.

4 Documentation and Records

BH shall prepare and maintain adequate documentation of the HRPP and IRB activities. Records must be accessible for inspection and copying by authorized representatives of the FDA, OHRP, sponsors, and other authorized entities at reasonable times and in a reasonable manner.

4.1 HRPP Records

HRPP records include, but are not limited to:

1. Written operating procedures.
2. Training records for HRPP and IRB staff.
3. Quality Assurance reviews and reports.
4. Records of audits and investigations conducted by regulatory authorities.
5. Reports and other documentation related to accreditation.

4.2 IRB Records

IRB records include, but are not limited to:

1. Written operating procedures.
2. IRB membership rosters.
3. Training records. The HRPP Integrity and Education Specialist maintains accurate records listing research investigators, IRB members, and IRB staff that have fulfilled the facility's human subject training requirements. Electronic and hard copies of documentation are maintained in the official IRB records located in the IRB Office.
4. IRB correspondence (other than protocol related).
5. IRB Study Files
6. Documentation of Emergency Exemption from Prospective IRB Approval (21 CFR 56.104(c)).
7. Documentation of Exceptions from Informed Consent Requirements for Emergency Use of a Test Article (21 CFR 50.23).
8. Documentation of exemptions.
9. Documentation of convened IRB meetings minutes.

10. Documentation of review by another institution's IRB when appropriate.
11. Documentation of cooperative review agreements, e.g. Memoranda of Understanding (MOUs).
12. Federal Wide Assurances.

4.3 IRB Study Files

The IRB maintains on-line study files via IRBNet for each research application (protocol) that it receives for review. Protocols will be assigned a unique identification number by the electronic system for tracking purposes. Accurate records are maintained of all communications to and from the IRB in the study file. The study file for each research protocol includes, but is not limited to the following:

1. Protocol and all other documents submitted as part of a new protocol application.
2. Protocol and all other documents submitted as part of a request for continuing review or closure of research application. This also includes progress reports, statements of significant new findings provided to participants, reports of problems with the research.
3. Documents submitted and reviewed after the study has been approved, including reports of modifications to research/amendments and unanticipated problem reports.
4. Copy of IRB-approved Consent Form
5. DHHS-approved sample consent form document and protocol, when they exist
6. IRB reviewer forms and documentation verifying scientific review (where applicable).
7. Documentation of type of IRB review.
8. For expedited review, documentation of any determinations required by the regulations and protocol-specific findings supporting those determinations, including: waiver or alteration of the consent process, research involving pregnant women, fetuses, and neonates, research involving prisoners, and research involving children.
9. Documentation of all IRB review actions.
10. Notification of expiration of IRB approval to the PI and instructions for submitting relevant continuing review materials.
11. Notification of suspension of research.
12. Correspondence pertaining to appeals.

13. Copies of approval letters and forms that describe what Principal Investigator must have before beginning the study.
14. IRB correspondence to and from research investigators.
15. All other IRB correspondence related to the research.
16. for devices, documentation of determination by IRB of significant risk/non-significant risk/exempt and a report of prior investigations
17. Reports of unanticipated problems involving risk to subjects or others
18. DSMB reports
19. Protocol Deviation reports
20. Reports of Unanticipated Adverse Device Events
21. Documentation from external inspections and audits.

4.4 The IRB Minutes

Proceedings are written and available for review by the next regularly scheduled IRB meeting date. Once approved by the members at a subsequent IRB meeting, the minutes must not be altered by anyone including a higher institutional authority.

Minutes of IRB meetings must contain sufficient detail to show:

1. Attendance
 - a. Names of members present
 - b. Names of members or alternate members who are participating through videoconference or teleconference and documentation that those attending through videoconferencing or teleconferencing received all pertinent material prior to the meeting and were able to actively and equally participate in all discussions
 - c. Names of alternates attending in lieu of specified (named) absent members. (Alternates may substitute for absent members only as designated on the official IRB membership roster)
 - d. Names of staff present
 - e. Names of consultants present
 - f. Name of investigators present

g. Names of guests present

Note: The attendance list shall include those members present at the meeting. The minutes will indicate, by name, those members who enter or leave the meeting. The vote on each action will reflect those members present for the vote on that item. Members who recuse themselves because of conflict of interest are listed by name.

2. The presence of a quorum throughout the meeting, including the presence of one member whose primary concern is in a non-scientific area
3. Business Items discussed
4. Continuing Education
5. Actions taken, including separate deliberations, actions, and votes for each protocol undergoing initial review, continuing review, or review of modifications by the convened IRB
6. Votes on these actions (Total Number Voting; Number voting for; Number voting against; Number abstaining; Number of those recused)
7. Basis or justification for these actions including required changes in research
8. Summary of controverted issues and their resolution
9. Approval period for initial and continuing approved protocols, including identification of research that warrants review more often than annually and the basis for that determination
10. Risk level of initial and continuing approved protocols
11. Review of interim reports, e.g. unanticipated problems or safety reports; amendments; report of violation/deviations; serious or continuing non-compliance; suspensions/terminations, etc.
12. Review of Data and Safety Monitoring Board (DSMB) summary
13. Review of Plans for Data and Safety Monitoring
14. Justification of deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document.
15. Protocol-specific documentation that the research meets the required criteria [45 CFR 46.116(d)] when approving a consent procedure that does not include or that alters some or all of the required elements of informed consent, or when waiving the requirement to obtain an informed consent

16. Protocol-specific documentation that the research meets the required criteria [45 CFR 46.117(c)] when the requirements for documentation of consent are waived
17. When approving research that involves populations covered by Subparts B, C, or D of 45 CFR 46, the Minutes will document the IRB's justifications and findings regarding the determinations stated in the Subparts or the IRB's agreement with the findings and justifications as presented by the investigator on IRB forms.
18. Special protections warranted in for other groups of subjects who are likely to be vulnerable to coercion or undue influence, such as mentally disabled persons, or economically or educationally disadvantaged persons, regardless of source of support for the research.
19. Significant risk/non-significant risk device determinations.
20. Determinations of conflict of interest.
21. Identification of any research for which there is need for verification from sources other than the investigator that no material changes are made in the research.
22. A list of research approved since the last meeting utilizing expedited review procedures.
23. An indication that, when an IRB member has a conflicting interest (see Section 2.8) With the research under review, the IRB member was not present during the final deliberations or voting on the proposal, and that the quorum was maintained.
24. Key information provided by consultants will be documented in the minutes or in a report provided by the consultant

A copy of the IRB-approved minutes for each IRB meeting will be distributed to the Institutional Official. The IRB minutes, once approved, may not be altered by any persons of authority except by the IRB Chair with the concurrence and approval of the convened IRB.

4.5 IRB Membership Roster

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

1. Name
2. Earned degrees
3. Affiliated or non-affiliated status (neither the member nor an immediate family member of the member may be affiliated with the institution)

4. Status as scientist (physician-scientist, other scientist, non-scientist or social behavioral scientist). For purposes of this roster, IRB members with degrees in health sciences (ex. physicians, nurses, and pharmacists), doctoral degrees in social-behavioral sciences or in another scientific field are designated as scientists.
5. Indications of experience, such as board certifications or licenses sufficient to describe each member's chief anticipated contributions to IRB deliberations.
6. Representative capacities of each IRB member; which IRB member is a prisoner representative (as required by Subpart C), and which IRB members are knowledgeable about or experienced in working with children, pregnant women, cognitively impaired individuals, and other vulnerable populations locally involved in research.
7. Role on the IRB (Chair, Vice-Chair, etc.)
8. For alternate members, the primary member or class of members for whom the member could substitute
9. Relationship (e.g., employment) between the individual IRB member and the organization

The HRPP office must keep IRB membership roster current. The Director of the HRPP office must promptly report changes in IRB membership to the Office for Human Research Protections, Departments of Health and Human Services.

4.6 Documentation of Exemptions

Documentation of verified exemptions consists of the Director's or IRB reviewer's citation of a specific exemption category and written concurrence that the activity described in the investigator's request for satisfies the conditions of the cited exemption category as detailed in Section 3.3. The exempt determination is recorded on-line.

4.7 Documentation of Expedited Reviews

IRB records for initial and continuing review by the expedited procedure must include: the specific permissible category; that the activity described by the investigator satisfies all of the criteria for approval under expedited review; the approval period and any determinations required by the regulations including protocol-specific findings supporting those determinations.

4.8 Access to IRB Records

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

1. All IRB records are maintained in a secure electronic format or kept secure in locked filing cabinets.

2. Ordinarily, access to all IRB records is limited to the Director, IRB Chair, IRB members, HRPP/IRB staff, authorized institutional officials, and officials of Federal and state regulatory agencies (OHRP, FDA). Research investigators are provided reasonable access to files related to their research. Appropriate accreditation bodies are provided access and may recommend additional procedures for maintaining security of IRB records. All other access to IRB records is limited to those who have legitimate need for them, as determined by the IO and Director.
3. Records are accessible for inspection and copying by authorized representatives of Federal regulatory agencies during regular business hours.
4. Paper Records may not be removed from the IRB Office; however, the IRB staff will provide copies of records to authorized personnel if requested.
5. All other access to IRB study files is prohibited.

4.9 Record Retention

IRB records (as described in Section 4.2) must be retained by the facility for at least three (3) years. IRB Minutes are retained indefinitely as required by institutional policy. Records are maintained electronically on a secured web-site, on a secured S-drive, in locked files within the IRB office area, or archived in a secure record storage facility. A record is maintained describing the location of all archived files.

IRB Records pertaining to research, which is conducted, must be retained for at least three years after completion of the research. IRB records not associated with research or for protocols cancelled without participant enrollment will be retained at the facility for at least 3 years after closure.

After that time records may be shredded or otherwise destroyed.

5 Obtaining Informed Consent from Research Subjects

No investigator conducting research under the auspices of BH may involve a human being as a subject in research without obtaining the legally effective informed consent of the subject or the subject's legally authorized representative unless a waiver of consent has been approved by the IRB in accordance with Section 5.9 of these procedures. Except as provided in Section 5.10 of these procedures, informed consent must be documented by the use of a written consent form approved by the IRB.

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

The following procedures describe the requirements for obtaining consent from participants in research conducted under the auspices of BH.

5.1 Definitions

Legally Authorized Representative means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. [45CFR46.102(c)] Consent may be obtained from a court appointed guardian of the person **or** a health care agent appointed by the person in a Health Care Proxy or similar document that complies with the requirements of Massachusetts law, (M.G.L., Chapter 201D, including a durable power of attorney for health care. In the absence of a guardian or Health Care Agent, consult BH [Clinical Operations Policy](#) CO 9.100, Informed Consent and Health Care Decisions. Special rules apply when a potential subject is under the care or custody of a state agency.

5.2 Basic Requirements

The requirement to obtain the legally effective informed consent of individuals before involving them in Research is one of the central protections provided for by the Federal regulations and BH HRPP. Investigators are required to obtain legally effective informed consent from a subject or the subject's Legally Authorized Representative. When informed consent is required, it must be sought prospectively, and properly documented.

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

Informed consent is more than just a signature on a form. It is a process of information exchange to include reading and signing the informed consent document. The informed consent process is the critical communication link between the prospective Human Subject and an Investigator, beginning with the initial approach of an Investigator and continuing through the completion of the Research study. Investigators must have received the appropriate training and be knowledgeable about the study Protocol in order that they may answer

questions to help provide understanding to the study participant or potential study potential study participant.

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

If someone other than the investigator conducts the interview and obtains consent from a subject, the investigator needs to formally delegate this responsibility, and the person so delegated must have received appropriate training to perform this activity. The person so delegated must be knowledgeable about the research to be conducted and the consenting process, and must be able to answer questions about the study. See Section 13 for further description on delegation of tasks and categories of individuals generally considered acceptable for delegation of key responsibilities.

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

5.3 Informed Consent Process

Informed consent must be obtained under the following circumstances:

1. Informed consent may only be obtained from subjects who have the legal and mental capacity to give consent. For subjects without that capacity, consent must be obtained from a legal guardian or a legally authorized representative.
2. Special rules will apply if the subject is a client of a state agency, such as the Department of Mental Retardation or the Department of Mental Health. Consult with the Research Integrity Officer or legal counsel for additional information.
3. The informed consent process shall be sought under circumstances that provide the subject (or legally authorized representative) with sufficient opportunity to consider whether or not to participate.
4. The informed consent process shall be sought under circumstances that minimize the possibility of coercion or undue influence.
5. The informed consent information must be presented in language that is understandable to the subject (or legally authorized representative). To the extent possible, the language should be understandable by a person who is educated to 8th grade level and layman's terms shall be used in the description of the research.
6. For subjects whose native language is not English, informed consent must be obtained in a language that is understandable to the subject (or the subject's legally authorized representative). In accordance with this policy, the IRB requires that informed consent conferences include an interpreter when the prospective subject does not understand

[Services](#) (CO 10.310) must be followed.

7. The informed consent process may not include any exculpatory language through which the subject is made to waive, or appear to waive any of the subject's legal rights or through which the investigator, the sponsor, BH or BH employees or agents are released from liability for negligence, or appear to be so released.
8. The PI is responsible for ensuring that each prospective subject is adequately informed about all aspects of the research and understands the information provided.

5.4 Basic Elements of Informed Consent

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

1. A statement that the **study involves research**, an explanation of the **purposes** of the research and the expected duration of the subject's participation, a description of the **procedures** to be followed, and identification of any procedures which are experimental; a description of any reasonably foreseeable **risks** or discomforts to the subject;
2. A description of any **benefits** to the subject or to others which may reasonably be expected from the research;
3. A disclosure of appropriate **alternative procedures** or courses of treatment, if any, that might be advantageous to the subject;
4. A statement describing the extent, if any, to which **confidentiality** of records identifying the subject must be maintained;
5. For research involving more than minimal risk, an explanation as to the availability of medical treatment in the case of **research-related injury**, including who will pay for the treatment and whether other financial compensation is available;
6. An **explanation of whom to contact** on the research team for answers to pertinent questions about the research or to voice concerns or complaints about the research, and whom to contact in the event of a research-related injury to the subject;
7. **Contact information for the IRB** to obtain answers to questions about the research; to voice concerns or complaints about the research; to obtain answers to questions about their rights as a research participant; in the event the research staff could not be reached; and in the event the subject wishes to talk to someone other than the research staff.

8. A statement that participation is **voluntary**, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled;
9. For **FDA-regulated studies**, the possibility that the Food and Drug Administration may inspect the records needs to be included in the statement regarding subject confidentiality.
10. For applicable FDA-regulated clinical trials, the following statement regarding the clinical trials registry databank: *"A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."*

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

1. A statement that the particular treatment or procedure may involve risks to the subject, which are currently unforeseeable. (For example: Include when the research involves investigational test articles or other procedures in which the risks to subjects is not well known.)
2. A statement that if the subject is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus, which are currently unforeseeable. (For example: Include when the research involves pregnant women or women of childbearing potential and the risk to fetuses of the drugs, devices, or other procedures involved in the research is not well known.)
3. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent. (For example: Include when there are anticipated circumstances under which the investigator may terminate participation of a subject.)
4. Any additional costs to the subject that may result from participation in the research. (For example: Include when it is anticipated that subjects may have additional costs.)
5. The consequences of a subject's decision to withdraw from the research. (For example: Include when withdrawal from the research is associated with adverse consequences.)
6. Procedures for orderly termination of participation by the subject. (For example: Include when the protocol describes such procedures.)
7. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject. (For example: Include when the research is long term and interim information is likely to be developed during the conduct of the research.)

8. The approximate number of subjects involved in the study. (For example: Include when the research involves more than minimal risk.)
9. The amount and schedule of any compensation/payment to subjects.
10. The consent should include a description of data retention upon withdrawal and the potential for partial withdrawal from a clinical trial (For example: withdrawal from interventional component of study but agreement to allow collection of follow up data). See Section 5.8 and [FDA Guidance: Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials](#), [OHRP Guidance: Guidance on Withdrawal of Subjects: Data Retention and Other Related Issues](#).

5.5 Documentation of Informed Consent

Except as provided in Section 5.10 of this document, informed consent must be documented by the use of a written consent form approved by the IRB.

1. Informed consent is documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent.
2. A copy of the signed and dated consent form must be given to the person signing the form.
3. The consent form may be either of the following:

A written consent document that embodies the basic and required additional elements of informed consent. The consent form must be the currently approved version and must bear the IRB stamp. The consent form may be read to the subject or the subject's legally authorized representative, but the subject or representative must be given adequate opportunity to read it before it is signed; or

A short form consent document may be utilized when a long form is not available in the participants language. IRB-approved short form consent documents are available in other languages on the IRB website. Section 5.6.2 for a description of the short form consent process.

5.6 Special Consent Circumstances

5.6.1 Expected enrollment of subjects with limited English-language proficiency:

It is essential that non-English speaking individuals and those individuals with limited English language proficiency have equal access to research protocols. Since research protocols offer a potential for direct benefit that may only be available within the context of the research, the exclusion of non-English speaking individuals becomes ethically problematic. Baystate Health

provides qualified interpreters and certified translations through the Interpreter and Translation Services Department.

Per regulation, the informed consent process must be done in a language that is understandable to the subject. Based on our patient population, the BH IRB requires that most consent forms (CF) and subject research materials be fully translated into Spanish. The HRPP/IRB staff facilitate this process by coordinating the translation process. If a researcher anticipates enrollment of subjects in other languages, the research should contact the HRPP/IRB staff to facilitate translation of the consent document into the necessary language.

Researchers should plan in advance so that an interpreter is available as needed for the consent process and ongoing interactions with the subject. To ensure the accuracy of interpretation, unless a provider is a native fluent speaker of the patient's language, an interpreter must be arranged for by contacting Interpreter and Translation Services. For further information, please see the [IRB Fact Sheet: Translations and Use of Interpreters](#).

5.6.2 Unexpected enrollment of subjects with limited English-language proficiency:

If a potential subject with limited English language proficiency presents unexpectedly, there may not be an IRB-approved written translation of the consent document available. In these cases, the investigator should carefully consider the ethical and legal ramifications of enrolling subjects when a language barrier exists. If the subject does not clearly understand the information presented at the signing of the consent document or in subsequent discussions, his/her consent may not be informed, and therefore, not effective.

Should the investigator choose to proceed with the consent process, a short-form consent document (available on eWorkplace in several languages) may be utilized. The short form consent contains a summary of the informed consent elements found in the consent long form. The short form consent is to be administered with an oral presentation/summary of the IRB approved long consent form. As with the long form, when the short form is used, an interpreter arranged for through Interpreter and Translation Services must be present in accordance with hospital policy. The short form is then signed by the subject and the witness. The consent long form is signed by the witness and the person obtaining consent. A copy of both the short form and consent long form are given to the subject. A full written translation of the consent long form should be requested from Interpreter and Translation Services and provided to the participant as soon as it becomes available.

5.6.3 Enrollment of subjects unable to read or sign the consent document

When a potential subject is unable to read a written consent form (such as blind or illiterate subjects, or subjects with a physical injury that prohibits their ability to provide a written signature), consent may be documented as follows, provided the potential subject (1) retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained verbally and (2) is able to indicate approval or disapproval to study entry.

If the subject is unable to read the written consent form, the consent form must be read to the subjects and the subjects must be given an opportunity to ask questions. An audio or videotape approved by the IRB may be used.

If capable of doing so, the subject signs, or marks an X to signify consent. If that is not possible, the subject will provide verbal consent. The person obtaining consent and a witness will sign the written consent form with a statement that documents that an oral process was used and, if necessary, that the subject gave verbal consent. The consent process will also be documented in the medical record if possible or alternatively in the research subject record. Copies of the executed consent form are provided to the subject and placed in the medical record (when the subject is a patient). If an audio or videotape is available, the subject should be provided a copy.

5.7 Consent Monitoring

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

Such monitoring may be particularly warranted for:

1. High risk studies
2. Studies that involve particularly complicated procedures or interventions
3. Studies involving highly vulnerable populations (e.g., ICU patients, children)
4. Studies involving study staff with minimal experience in administering consent to potential study participants, or
5. Other situations when the IRB has concerns that consent process is not being conducted appropriately.

Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with a particular investigator or a research project.

If the IRB determines that consent monitoring is required, the convened IRB or the IRB Chair and the Director will develop a monitoring plan. The consent monitoring may be conducted by HRPP/IRB staff, IRB members or another party, either affiliated or not with the institution. The PI will be notified of the IRB's determination and the reasons for the determination. Arrangements will be made with the PI for the monitoring of the consent process for a specified number of subjects. When observing the consent process, the monitor will determine:

- Whether the informed consent process was appropriately completed and documented,

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

Following the monitoring, a report of the findings will be submitted to the IRB, which will determine whether any additional action is necessary.

5.8 Subject Withdrawal or Termination

For a variety of reasons, a subject enrolled in a research study may decide to withdraw from the research, or an investigator may decide to terminate a subject's participation in research regardless of whether the subject wishes to continue participating. In these circumstances, questions sometimes arise about: (1) whether the investigator may use, study, or analyze already collected data about the subject who withdraws from the research or whose participation is terminated by the investigator; and (2) whether the investigator can continue to obtain data about the subject and if so, under what circumstances. The following addresses these and related questions. Investigators must plan for the possibility that subjects will withdraw from research and include a discussion of what withdrawal will mean and how it will be handled in their research protocols and consent documents.

Regulatory requirements regarding the retention and use of data after subject withdrawal or termination differ between research subjects to FDA regulations and that not subject to FDA regulations. Under applicable FDA law and regulations, data collected on human subjects enrolled in an FDA-regulated clinical trial up to the time of subject withdrawal must remain in the trial database in order for the study to be scientifically valid. For research not subject to FDA regulations, investigators, in consultation with the funding agency, can choose to honor a research subject's request that the investigator destroy the subject's data or that the investigator exclude the subject's data from any analysis.

When seeking informed consent from subjects, the following information regarding data retention and use must be included:

- For FDA-regulated clinical trials, when a subject withdraws from a study, the data collected on the subject to the point of withdrawal remain part of the study database and may not be removed. The consent document cannot give the subject the option of having data removed.
- For research not subject to FDA regulations, the investigator should inform subjects whether the investigator intends to either: (1) retain and analyze already collected data relating to the subject up to the time of subject withdrawal; or (2) honor a research subject's request that the investigator destroy the subject's data or that the investigator exclude the subject's data from any analysis.

Sometimes, a subject wants to withdraw from the primary interventional component of a study, but is willing to allow the investigator to continue other research activities described in the IRB-approved protocol and informed consent document that involve participation of the subject, such as: (1) obtaining data about the subject through interaction with the subject (e.g., through follow-up interviews, physical exams, blood tests, or radiographic imaging); or (2) obtaining identifiable private information from the subject's medical, educational, or social services agency records or from the subject's healthcare providers, teachers, or social worker. When a subject's withdrawal request is limited to discontinuation of the primary interventional component of a research study, research activities involving other types of participation for which the subject previously gave consent may continue. Investigator should ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through noninvasive chart review, and address the maintenance of privacy and confidentiality of the subject's information.

If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous paragraph, the investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). IRB approval of consent documents would be required.

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

For further discussion on this topic, please see the [FDA Guidance: Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials](#), and the [OHRP Guidance: Guidance on Withdrawal of Subjects: Data Retention and Other Related Issues](#).

5.9 Waiver of Informed Consent

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

- (a) The research involves no more than minimal risk to the subjects;
- (b) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(c) The research could not practicably be carried out without the waiver or alteration; and

(d) Whenever appropriate, the subjects must be provided with additional pertinent information after participation.

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

(a) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:

1. Public benefit or service programs
2. Procedures for obtaining benefits or services under those programs
3. Possible changes in or alternatives to those programs or procedures; or
4. Possible changes in methods or levels of payment for benefits or services under those programs.

(b) The research could not practicably be carried out without the waiver or alteration.

FDA regulations do not provide for waivers of informed consent except in emergency situations (See Section 7.5 and 7.7). There is an allowance for waiver of the requirement for a signed consent form (waiver of documentation of consent) for certain FDA-regulated studies [21 CFR 56.109(c)] as described below. This is most commonly applied to minimal risk screening activities. See [FDA Guidance: Screening Tests Prior to Study Enrollment](#).

5.10 Waiver of Documentation of Informed Consent

For non-FDA-regulated research, the IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either that the:

1. Only record linking the subject and the research would be the consent document and the principle risk would be potential harm resulting from a breach of confidentiality; or
Note: Subjects must be asked whether they want documentation linking them with the research, and their wishes must govern. (Example: domestic violence research where the primary risk is discovery by the abuser that the subject is talking to researchers.)
2. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. Procedures such as non-sensitive surveys, questionnaires and interviews generally do not require written consent when conducted by non-researchers.

For FDA-regulated research, there is an allowance for waiver of the requirement for a signed consent form for certain FDA-regulated studies [21 CFR 56.109(c)] as described below. This is most commonly applied to minimal risk screening activities. See [FDA Guidance: Screening Tests Prior to Study Enrollment](#).

1. The IRB may, for some or all subjects, waive the requirement that the subject, or the subject's legally authorized representative, sign a written consent form if it finds that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context.
2. In cases where the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

When the documentation requirement is waived (both FDA and non-FDA), the IRB requires the investigator to provide in the application materials a script or a written summary of the information to be communicated to the subject, and the IRB will consider whether to require the investigator to provide subjects with a written statement regarding the research.

6 Vulnerable Subjects in Research

When some or all of the participants in a research conducted under the auspices of Baystate are likely to be vulnerable to coercion or undue influence or have diminished decision-making capacity, the research must include additional safeguards to protect the rights and welfare of these participants. The IRB must ensure that all of the regulatory requirements for the protection of vulnerable subjects are met and that appropriate additional protections for vulnerable subjects are in place.

The following procedures describe the requirements for involving vulnerable participants in research under the auspices of Baystate.

6.1 Definitions

Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. According to Massachusetts State Law, a person who has reached the age of majority (eighteen years) may consent for his or her own medical care at the age of eighteen. Therefore, the Baystate IRB generally defines children as persons under eighteen years of age. Certain statutes and case law, however, provide exceptions to this general rule and allow a person under the age of eighteen to give consent under certain circumstances. For example:

- emancipated minors - Massachusetts law enumerates certain categories of individuals who, although under the age of 18, have the right to make medical decisions on their own behalf, such as minors who are married, widowed or divorced, minors who are parents, etc:
- mature minors – Massachusetts law recognizes that some minors may be sufficiently “mature” to give consent to medical treatment, even though they do not qualify as emancipated
- certain minors seeking care for drug addiction or sexually transmitted diseases

For a complete discussion of these rules under Massachusetts laws, see [Baystate’s Clinical Operations Policy on Treatment of Minors, CO 9.101](#).

Massachusetts law does not specifically address consent of children who have the ability to consent to research, where a protocol is intended or expected to include minors who fall within one or more of the exceptions, the Baystate IRB will review issues of consent related to enrollment of these children in research on a case-by-case basis.

NOTE: For research conducted in jurisdictions other than Massachusetts, the research must comply with the laws regarding the legal age of consent in all relevant jurisdictions. The

Research Integrity Officer, in consultation with legal counsel to Baystate, will provide assistance with regard to the laws in other jurisdictions.

Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. In Massachusetts a “Guardian” of a minor has the duty and authority to act in the best interests of the minor, subject to residual parental rights and responsibilities, to make important decisions in matters having a permanent effect on the life and development of the minor and to be concerned with his or her general welfare. (M.G. Chapter 201).

NOTE: For research conducted in jurisdictions other than Massachusetts, the research must comply with the laws regarding guardianship in all relevant jurisdictions. The Research Integrity Officer, in consultation with legal counsel to Baystate, will provide assistance with regard to the laws in other jurisdictions.

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

Fetus is the product of conception from the time of implantation until delivery.

Viable fetus is now termed a “viable neonate.”

Nonviable fetus is a fetus ex utero that, although living, is not able to survive to the point of independently maintaining heart and respiration. **NOTE:** *In 45 CFR 46 Subpart B, this definition is used as the definition of a non-viable neonate.*

Dead fetus is a fetus which exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord if still attached.

Neonate means newborn.

Viable neonate means being able, after delivery, to survive to the point of being independently maintaining heart and respiration (given the benefit of available medical therapy).

Non-viable neonate means the same as a non-viable fetus.

In vitro fertilization is any fertilization of human ova, which occurs outside the body of a female, either through a mixture of donor human sperm and ova or by any other means.

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

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

[Guidance](#) expands upon the regulatory definition to clarify that individuals are prisoners if they are in any kind of penal institution, such as a prison, jail, or juvenile offender facility, and their ability to leave the institution is restricted. This includes untried persons who are detained pending judicial action and individuals detained in a residential facility for court-ordered substance abuse treatment or a psychiatric facility as a form of sentencing or alternative to incarceration. Consult with the HRPP if in question.

6.2 Involvement of Vulnerable Populations

When some or all of the participants in a protocol are likely to be vulnerable to coercion or undue influence, the IRB should include additional safeguards to protect the rights and welfare of these participants. Some of the vulnerable populations that might be involved in research include children, pregnant women, fetuses, neonates, prisoners, or adults who lack the ability to consent, students, employees, or homeless persons.

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

45 CFR 46 has additional subparts designed to provide extra protections for vulnerable populations which also have additional requirements for IRBs.

Subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research

Subpart C - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects

Subpart D - Additional Protections for Children Involved as Subjects in Research

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

Under Baystate's FWA the subparts only apply to DHHS-funded research and research funded by another federal agency that requires compliance with the subparts (FDA regulations include Subpart D, which applies to all FDA-regulated research). The following policies and procedures,

which are based on the subparts, apply to all research regardless of funding. The individual sections describe how the subparts apply to DHHS-funded research.

6.3 Responsibilities

1. The PI is responsible for identifying the potential for enrolling vulnerable subjects in the research proposal. The PI is responsible for identifying patients who are at risk for impaired decisional capacity or are otherwise potentially vulnerable and who are being asked to participate in a research study with greater than minimal risk.
2. The IRB shall include representation, either as members or ad hoc consultants, individual(s) interested in or who have experience with the vulnerable populations involved in a research proposal.
3. The IRB reviews the PI's justifications for including vulnerable populations in the research to assess appropriateness of the research proposal.
4. The IRB must ensure that additional safeguards have been included in each study to protect the rights and welfare of vulnerable subjects as needed at the time of initial review of the research proposal.
5. Information reviewed as part of the continuing review process should include the number of participants considered as members of specific vulnerable populations.
6. For studies that do not have or are not required to have a Data and Safety Monitoring Board (DSMB) or a Data Monitoring Committee and have entered vulnerable subjects, the IRB needs to carefully review the safety monitoring plan.
7. The IRB should be knowledgeable about and experienced in working with populations who are vulnerable to coercion and undue influence. If the IRB requires additional qualification or expertise to review a protocol, it should obtain consultation.

6.4 Procedures

6.4.1 Initial Review of Research Proposal:

1. The PI should identify the potential to enroll vulnerable subjects in the proposed research at initial review and provide the justification for their inclusion in the study.
2. The IRB evaluates the proposed plan for consent of the specific vulnerable populations involved. If the research involves adults unable to consent, the IRB evaluates the proposed plan for permission of legally authorized representatives.
3. The IRB evaluates and approves the proposed plan for the assent of participants.

4. The IRB evaluates the research to determine the need for additional protections and consider the use of a data and safety monitoring board or data monitoring committee as appropriate.
5. The PI should provide appropriate safeguards to protect the subject's rights and welfare, which may include the addition of an independent monitor. The independent monitor is a qualified individual not involved in the research study who will determine the subject's capacity to provide voluntary informed consent.
6. The IRB assess the adequacy of additional protections for vulnerable populations provided by the PI.

6.4.2 Continuing Review and Monitoring

At Continuing review the PI should identify the number of vulnerable subjects enrolled and any that needed an independent monitor in the progress report.

6.5 Research Involving Pregnant Women, Human Fetuses and Neonates

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

6.5.1 Research Involving Pregnant Women or Fetuses

6.5.1.1 Research Not Funded by DHHS

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

Pregnant women or fetuses may be involved in research not funded by DHHS and involving more than minimal risk to fetuses if all of the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus;
3. Any risk is the least possible for achieving the objectives of the research;
4. If the research holds out the prospect of direct benefit to the pregnant woman or the prospect of a direct benefit both to the pregnant woman and the fetus, then the

5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or if the pregnancy resulted from rape or incest.
6. Each individual providing consent under paragraph 4 or 5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. For children who are pregnant, assent and permission are obtained in accord with the provisions of permission and assent;
 - a. Note: In general, in Massachusetts, minors who are pregnant or believe themselves to be pregnant are considered emancipated. Parental permission and assent are in most cases unnecessary. See CO 9.101 – Treatment of Minors. When the research may include pregnant minors from other states, the Research Integrity Officer should be consulted to provide an advisory opinion on relevant state law.
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
10. Individuals engaged in the research will have no part in determining the viability of a neonate.

6.5.1.2 Research Funded by DHHS

For DHHS-funded research, 45 CFR Subpart B applies to all research involving pregnant women. Under 45 CFR Subpart B, pregnant women or fetuses may be involved in research funded by DHHS if **all** of the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risk to pregnant women and fetuses.
2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
3. Any risk is the least possible for achieving the objectives of the research;

4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, then the consent of the pregnant woman is obtained in accord with the provisions for informed consent.
5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or if the pregnancy resulted from rape or incest.
6. Each individual providing consent under paragraph 4 or 5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. For children who are pregnant, assent and permission are obtained in accord with the provisions of Subpart D;
 - a. Note: In general, in Massachusetts, minors who are pregnant or believe themselves to be pregnant are considered emancipated. Parental permission and assent are in most cases unnecessary. See CO 9.101 – Treatment of Minors. When the research may include pregnant minors from other states, the Research Integrity Officer should be consulted to provide an advisory opinion on relevant state law.
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
10. Individuals engaged in the research will have no part in determining the viability of a neonate.

6.5.2 Research Involving Neonates

Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
2. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
3. Individuals engaged in the research will have no part in determining the viability of a neonate.

4. The requirements of Neonates of Uncertain Viability or Nonviable Neonates (see below in this section) have been met as applicable.
5. Additionally, per Massachusetts law (M.G.L.c.112,sec.12J), research involving fetuses or neonates must be conducted for the purpose of developing, comparing or improving diagnostic or therapeutic fetal or neonatal interventions to improve the viability or quality of life of fetuses, neonates and children

6.5.2.1 Neonates of Uncertain Viability.

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

The IRB determines that:

1. The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or
2. The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
3. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with the provisions of permission and assent, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

6.5.2.2 Nonviable Neonates.

After delivery, nonviable neonates may not be involved in research covered by this subpart unless all of the following additional conditions are met:

1. Vital functions of the neonate will not be artificially maintained;
2. The research will not terminate the heartbeat or respiration of the neonate;
3. There will be no added risk to the neonate resulting from the research;
4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and

5. The legally effective informed consent of both parents of the neonate is obtained in accord with the provisions of permission and assent, except that the waiver and alteration of the provisions of permission and assent do not apply.
6. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

6.5.2.3 Viable Neonates.

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of IRB Review Process and Research Involving Children (see Section 6.7) and only to the extent permitted under Massachusetts law. Per Massachusetts law (M.G.L.c.112,sec.12J) research involving fetuses or neonates must be conducted for the purpose of developing, comparing or improving diagnostic or therapeutic fetal or neonatal interventions to improve the viability or quality of life of fetuses, neonates and children.

NOTE: Research using **human embryonic stem cells** or **human genetic material**, including somatic cell nuclear transfer is permitted under Massachusetts law(M.G.L.Chapter 111L).

6.5.3 Research Involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material

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

The IRB will consider the application of Massachusetts laws regarding experimentation on human fetuses and research using human embryonic stem cells, consulting with legal counsel when necessary. **NOTE:** Massachusetts law (M.G.L.c.112, sec. 12J) requires consent of a parent or guardian for any experimentation that will involve a dead fetus.

If information associated with material described above in this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent sections of this manual are applicable.

6.5.4 Research Not Otherwise Approvable

6.5.4.1 Research Not Funded by DHHS

If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of

pregnant women, fetuses or neonates; and the research is not approvable under the above provisions, then the IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB may approve the research based on either:

1. That the research in fact satisfies the conditions of Section 6.2.2, as applicable; or
2. The following:
 - a. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;
 - b. The research will be conducted in accord with sound ethical principles; and
 - c. Informed consent will be obtained in accord with the provisions for informed consent and other applicable sections of this manual.

6.5.4.2 Research Funded by DHHS

DHHS-funded research that falls in this category must be approved by the Secretary of Health and Human Services. If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and the research is not approvable under the above provisions, then the research will be sent to OHRP for DHHS review.

6.6 Research Involving Prisoners

Prisoners are another of the three classes that are deemed so vulnerable to exploitation in research that there are special rules protecting them. In the past, prisoners were viewed as a convenient research population. They are housed in a single location, constitute a large and relatively stable population, and live a routine life. Unfortunately, all the things that make a prison and prisoners a convenient research population also make prisoners ripe for exploitation.

The concern Subpart C and this policy based on Subpart C attempt to address is whether prisoners have any real choice in participation in research, or whether incarceration prohibits free choice.

The following applies to all research involving prisoners, regardless of funding source. The requirements in this section are consistent with Subpart C of 45 CFR 46, which applies to DHHS-funded research.

6.6.1 Applicability

This policy applies to all biomedical and behavioral research conducted under the auspices of Baystate involving prisoners as subjects. Even though the IRB may approve a research protocol involving prisoners as subjects according to this policy, investigators are still subject to the policies and regulations of the Massachusetts Department of Corrections and the Sheriff of the County in which the prison or jail is located and any other applicable State or local laws, regulations or policies. [45 CFR 46.301] For research conducted at the Hampden County jail contact Dr. Martha Lyman, Director of Research, 413-858-0284 or martha.lyman@sdh.state.ma.us

6.6.2 Minimal Risk

The definition of minimal risk in the Subpart C is different than in the rest of the federal regulations. According to 45 CFR 46.303, *Minimal Risk* is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

6.6.3 Composition of the IRB

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

- A majority of the IRB (exclusive of prisoner members) must have no association with the prison(s) involved, apart from their membership on the IRB.
- At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one IRB, only one IRB need satisfy this requirement.
- The prisoner representative must be a voting member of the IRB. The prisoner representative may be listed as an alternative member who becomes a voting member when needed.

6.6.4 Review of Research Involving Prisoners

1. The prisoner representative must review research involving prisoners, focusing on the requirements in Subpart C.
2. The prisoner representative must receive all review materials pertaining to the research (same as the primary reviewer).
3. The prisoner representative must be present at a convened meeting when the research involving prisoners is reviewed. If the prisoner representative is not present, research cannot be reviewed or approved. The prisoner representative may attend the meeting

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.

4. The prisoner representative must present his/her review either orally or in writing at the convened meeting of the IRB when the research involving prisoners is reviewed.
5. Modifications.
 - a. Minor modifications to research may be reviewed using the expedited procedure described below, using either of the two procedures described based on the type of modification.
 - b. Modifications involving more than a minor change reviewed by the convened IRB must use the same procedures for initial review including the responsibility of the prisoner representative to review the modification and participate in the meeting (as described above).
6. Continuing review. Continuing review must use 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).
7. Expedited Review
 - a. Research involving interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied. The prisoner representative must concur with the determination that the research involves no greater than minimal risk. The prisoner representative must review the research as a reviewer, designated by the chair, or consultant. This may be as the sole reviewer or in addition to another reviewer, as appropriate. Review of modifications and continuing review must use the same procedures for initial review using this expedited procedure including the responsibility of the prisoner representative.
 - b. Research that does not involve interaction with prisoners (e.g. existing data, records review) may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied. Review by a prisoner representative is not required. The prisoner representative may review the research as a reviewer or consultant if designated by the IRB chair. Review of modifications and continuing review must use the same procedures as initial review.

6.6.5 Incarceration of Enrolled Subjects

If a participant becomes a prisoner while enrolled in a research study that was not reviewed according to Subpart C and Subpart C applies, the IRB must:

1. Confirm that the participant meets the definition of a prisoner.

2. Terminate enrollment or review the research study under Subpart C if it feasible for the participant to remain in the study.
3. Before terminating the enrollment of the incarcerated participant the IRB should consider the risks associated with terminating participation in the study. If the participant cannot be terminated for health or safety reasons, one of two options are available:
 - a. Keep the participant enrolled in the study and review the research under Subpart C. If some the requirements of Subpart C cannot be met, but it is in the best interests of the participant to remain in the study, keep the participant enrolled and inform OHRP of the decision along with the justification.
 - b. Remove the participant from the study and keep the participant on the study intervention under an alternate mechanism such as compassionate use, off label use, etc.
4. If a participant is incarcerated temporarily while enrolled in a study:
 - a. If the temporary incarceration has no effect on the study, keep the participant enrolled.
 - b. If the temporary incarceration has an effect on the study, handle according to the above guidance.

6.6.6 Additional Duties of the IRB

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

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

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

6.6.7 Certification to HHS

Under 45 CFR 46.305(c), the institution responsible for conducting research involving prisoners that is supported by HHS shall certify to the Secretary (through OHRP) that the IRB has made the seven findings required under 45 CFR 46.305(a). For all HHS conducted or supported research BH will send to OHRP a certification letter to this effect, which will also include the name and address of the institution and specifically identify the research protocol in question and any relevant HHS grant application or protocol. HHS conducted or supported research involving prisoners as subjects may not proceed until OHRP issues its approval in writing to BH on behalf of the Secretary under 45 CFR 46.306(a)(2).

Under its authority at 45 CFR 46.115(b), OHRP requires that the institution responsible for the conduct of the proposed research also submit to OHRP a copy of the research proposal so that OHRP can determine whether the proposed research involves one of the categories of research permissible under 45 CFR 46.306(a)(2), and if so, which one. The term "research proposal" includes the IRB-approved protocol, any relevant HHS grant application or proposal, any IRB

application forms required by the IRB, and any other information requested or required by the IRB to be considered during initial IRB review.

The above requirement does not apply to research that is not HHS conducted or supported.

6.6.8 Waiver for Epidemiology Research

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

1. In which the sole purposes are
 - a. To describe the prevalence or incidence of a disease by identifying all cases, or
 - b. To study potential risk factor associations for a disease, and
2. Where the IRB has approved the research and fulfilled its duties under 45 CFR 46.305(a)(2)–(7) and determined and documented that
 - a. The research presents no more than minimal risk and no more than inconvenience to the prisoner-subjects, and
 - b. Prisoners are not a particular focus of the research.
3. The specific type of epidemiological research subject to the waiver involves no more than minimal risk and no more than inconvenience to the human subject participants. The waiver would allow the conduct of minimal risk research that does not now fall within the categories set out in 45 CFR 46.306(a)(2).
4. The range of studies to which the waiver would apply includes epidemiological research related to chronic diseases, injuries, and environmental health. This type of research uses epidemiologic methods (such as interviews and collection of biologic specimens) that generally entail no more than minimal risk to the subjects.
5. In order for a study to be approved under this waiver, the IRB would need to ensure that, among other things, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of the data.

6.7 Research Involving Children

The following applies to all research involving children, regardless of funding source. The requirements in this section are consistent with Subpart D of 45 CFR 46, which applies to DHHS-funded research and Subpart D of 21 CFR 50, which applies to FDA-regulated research involving children.

6.7.1 Allowable Categories

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

1. **Research not involving greater than minimal risk.** [45 CFR 46.404] Research not involving physical or emotional risk greater than that ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (i.e., **minimal risk**).
 - Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 6.7.2 unless the criteria for a waiver of consent are satisfied.
2. **Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.** [45 CFR 46.405]
 - The risk is justified by the anticipated benefit to the subjects;
 - The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
 - Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 6.7.2.
3. **Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.** [45 CFR 46.406]
 - The risk represents a minor increase over minimal risk;
 - The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
 - The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition; and
 - Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 6.7.2.
4. **Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.** [45 CFR 46.407]

- Federally-funded research in this category must be approved by the Secretary of Health and Human Services.
- FDA-regulated research in this category must be approved by the Commissioner of Food and Drugs.
- For non-federally-funded, non-FDA research, the IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, and law). Based on the recommendation of the panel, the IRB may approve the research based on either:
 - That the research in fact satisfies the conditions of the previous categories, as applicable; or
 - The following:
 - The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
 - The research will be conducted in accordance with sound ethical principles; and
 - Informed consent will be obtained in accord with the provisions for informed consent and other applicable sections of this manual.
- Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 6.7.2.

6.7.2 Parental Permission and Assent

6.7.2.1 Parental Permission

The IRB must determine that adequate provisions have been made for soliciting the permission of each child's parent or guardian.

Parents or guardians must be provided with the basic elements of consent and any additional elements the IRB deems necessary, as described in Section 5.

The IRB may find that the permission of one parent is sufficient for research to be conducted under Categories 46.404 and 46.405 (1 & 2 above). The IRB's determination of whether permission must be obtained from one or both parents will be documented in the reviewer's worksheet when a protocol receives expedited review, and in meeting minutes when reviewed by the convened committee.

Consent from both parents is required for research to be conducted under Categories 46.406 and 46.407 (3 & 4 above) unless

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

For research not covered by the FDA regulation, the IRB may waive or alter the requirements for obtaining permission from a parent or legal guardian if:

- The research meets the provisions for waiver in Section 5.9 and 5.10; or
- If the IRB determines that the research protocol is designed for conditions or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children) provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and that the waiver is not inconsistent with Federal, State, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

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

Permission from parents or legal guardians must be documented in accordance with and to the extent required by Section 5.

Additional consent or approval may be required in the situations where a child is in the care or custody of a state agency.

6.7.2.2 Assent from Children

Because “assent” means a child’s affirmative agreement to participate in research, the child must actively show his or her willingness to participate in the research, rather than just complying with directions to participate and not resisting in any way. When judging whether children are capable of assent, the IRB is charged with taking into account the ages, maturity, and psychological state of the children involved. The IRB has the discretion to judge children’s capacity to assent for all of the children to be involved in a proposed research activity, or on an individual basis.

The IRB should take into account the nature of the proposed research activity and the ages, maturity, and psychological state of the children involved when reviewing the proposed assent procedure and the form and content of the information conveyed to the prospective subjects. For research activities involving adolescents whose capacity to understand resembles that of adults, the assent procedure should likewise include information similar to what would be provided for informed consent by adults or for parental permission. For children whose age and maturity level limits their ability to fully comprehend the nature of the research activity but

who are still capable of being consulted about participation in research, it may be appropriate to focus on conveying an accurate picture of what the actual experience of participation in research is likely to be (for example, what the experience will be, how long it will take, whether it might involve any pain or discomfort). The assent procedure should reflect a reasonable effort to enable the child to understand, to the degree they are capable, what their participation in research would involve.

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

At times there may be inconsistency between parent permission and child assent. If a child is capable of assent and the Institutional Review Board (IRB) requires that assent be sought, it must be obtained before the child can participate in the research activity. Thus, if the child dissents from participating in research, even if his or her parents or guardian have granted permission, the child's decision prevails.

However, the regulations state at [45 CFR 46.408\(a\)](#) that the IRB may waive the assent requirements if the intervention or procedure involved in the research holds out the prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of research. Conversely, if a child assents to participate in research, and parental permission has not been waived by the IRB, the permission of the parents or guardian is also required before the child can be enrolled in the research.

Even when the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances detailed in the Waiver of Informed Consent section of this manual.

6.7.2.3 The Assent Form

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

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

1. tell why the research is being conducted;
2. describe what will happen and for how long or how often;
3. say it's up to the child to participate and that it's okay to say no;

4. explain if it will hurt and if so for how long and how often;
5. say what the child's other choices are;
6. describe any good things that might happen;
7. say whether there is any compensation for participating; and
8. ask for questions.

For younger children, the document should be limited to one page if possible. Illustrations might be helpful, and larger type makes a form easier for young children to read. Studies involving older children or adolescents should include more information and may use more complex language.

6.7.3 Children Who are “Wards of the State”

Children who are “wards of the State” under Massachusetts law are under the care or custody of a state agency, usually the Massachusetts Department of Child and Family Services. These children can be included in research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition, only if such research is:

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

If the research meets the condition(s) above, an advocate must be appointed for each child who is a ward (one individual may serve as advocate for more than one child), in addition to any other individual acting on behalf of the child as legal guardian or in *loco parentis*.

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

Please Note: in some situations, special rules will apply:

Express permission to conduct research in a school setting will require the approval of the principal of the school.

In all cases when a child is under the care of the Massachusetts Department of Children and Family Services, a representative of the Department must be consulted to determine if additional consent or approval from the Department must be obtained even where the parent retains the ability to consent to medical treatment.

When a child is in the care of the Massachusetts Department of Youth Services, a representative of the Department must be consulted to determine if additional consent or approval from the Department must be obtained.

When a child is a client of the Massachusetts Department of Mental Health or the Department of Mental Retardation additional permissions are required. Consult with the Research Integrity Officer prior to proceeding.

6.8 Employees and Students as Subjects

When students and/or employees are being recruited as potential subjects, researchers must ensure that there are additional safeguards for these subjects. The voluntary nature of their participation must be primary and without undue influence on their decision. Researchers must emphasize to subjects that neither their academic status or grades, or their employment, will be affected by their participation decision.

To minimize coercion, investigators should avoid, whenever possible, the use of their students and employees in clinical protocols involving procedures which are neither therapeutic nor diagnostic.

Investigators should, whenever possible, solicit subjects through means such as bulletin board notices, flyers, advertisements in newspapers, and announcements in classes or laboratories other than their own. When entering a teaching environment to recruit students and conduct research, e.g. administer a survey, investigators should do so at the end of the instructional period to allow non-participating students the option of leaving the room, thereby alleviating pressure to participate.

The Dean or equivalent must grant permission for research where students are the intended subjects. The DIO must grant permission for research where residents are among the intended subjects. In most cases, permission from Chairs, Program Directors, Managers, or other leaders is necessary when staff from within their units of responsibility are among the intended subjects. This permission must be documented and included in the submission to the IRB. Electronic signature on the IRBNet application will in most instances suffice.

6.9 Persons with Impaired Decision Making Capacity

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

General Rule

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

1. When only incompetent persons or persons with impaired decision making capacity are suitable as research subjects. Competent persons are not suitable for the proposed

2. The proposed research entails no significant risks, tangible or intangible, or if the research presents some probability of harm, there must be at least a greater probability of direct benefit to the participant. Incompetent people or persons with impaired decision-making capacity are not to be subjects of research that imposes a risk of injury, unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.
3. Procedures have been devised to ensure that participant's representatives are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision making capacity. Health care agents (appointed under the MA Health Care Proxy Law or similar law) and next-of-kin, or guardians, must be given descriptions of both proposed research studies and the obligations of the person's representatives. They must be told that their obligation is to try to determine what the subject would do if competent, or if the subject's wishes cannot be determined, what they think is in the incompetent person's best interest.

6.9.1 IRB composition

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

6.9.2 Determination of Decision-Making Capacity

The decision-making capacity of a potential research subject should be evaluated when there are reasons to believe that the subject may not be capable of making voluntary and informed decisions about research participation.

The investigator and research staff must have adequate procedures in place for assessing and ensuring subjects' capacity, understanding, and informed consent or assent. The IRB will evaluate whether the proposed plan to assess capacity to consent is adequate.

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

For research that poses greater than minimal risk, the IRB may require investigators to use independent and qualified professionals to assess whether potential subjects have the capacity to give voluntary, informed consent. Even in research involving only minimal risk, the IRB may

require that the study include a capacity assessment if there are reasons to believe that potential subjects' capacity may be impaired. It is not necessary to require a formal capacity assessment by an independent professional for all potential research subjects with mental disorders.

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

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

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

In the event research participants become incompetent or impaired in decision making capacity after enrollment, the PI is responsible for notifying the IRB. The PI is responsible for developing a monitoring plan which follows the guidelines outlined above for incompetent and impaired decision making research participants.

6.9.2.1 Determining Capacity to Consent

Under Massachusetts law, the capacity to make health care decisions is defined as the ability to understand and appreciate the nature and consequences of health care decisions, including the benefits and risks of and alternatives to any proposed health care, and to reach an informed decision. M.G.L.c.201D, sec. 1. See also [BH Clinical Operations Policy: CO 9.100 Health Care Decisions](#).

Decisional capacity in the research context has been interpreted by the American Psychiatric Association as requiring:

- Ability to evidence a choice,
- Ability to understand relevant information,

- Ability to appreciate the situation and its likely consequences, and
- Ability to manipulate information rationally.

A range of professionals and methods may be utilized to assess capacity. In general the consent assessor should be a researcher or consultant familiar with dementias and qualified to assess and monitor capacity and consent in such subjects on an ongoing basis. The IRB will consider the qualifications of the proposed individual(s) and whether he or she is sufficiently independent of the research team and/or institution.

The majority of studies conducted at Baystate only allow enrolling subjects who have the capacity to consent. For studies that have been approved for enrolling vulnerable populations who may lack capacity to consent, there must be someone who is able to assess capacity of each potential subject to consent. The PI may determine after appropriate medical evaluation that the prospective research subject lacks decision-making capacity and is unlikely to regain it within a reasonable period of time. Additionally, if the reason for lack of capacity is because of mental illness then a psychiatrist or licensed psychologist must confirm this judgment and document in the individual's medical record in a signed and dated progress note.

6.9.3 Clients of the Department of Mental Health

When a person is a client of the Department of Mental Health, the regulations of the Department apply. (104 CMR 31.00 et seq., Research Authorization and Monitoring) Approval must be sought for research involving access to data or subjects within Department facilities or programs. Approval is obtained from the Local Research Review Committee or the Central Office Research Review Committee.

The requirements of the regulations are very detailed. Investigators are strongly encouraged to review the regulations in detail to ensure compliance.

6.9.4 Clients of the Department of Mental Retardation

When a person is a client of the Department of Mental Retardation, the regulations of the Department apply. (115 CMR 10.00 et seq., Research) Approval must be sought from the Research Review Committee of the Department.

The requirements of the regulations are very detailed. Investigators are strongly encouraged to review the regulations in detail to ensure compliance.

6.10 Informed Consent and Assent

Whenever the participants have the capacity to give consent (as determined by qualified professionals), informed consent should be obtained and documented in accordance with Section 5 above. When participants lack the capacity to give consent, investigators may obtain consent from the legally authorized representative of a subject (surrogate consent) as described below.

A person who is incompetent or has been determined to lack capacity to consent to participate in a research study should be informed about the trial to the extent compatible with the subject's understanding and, if possible, the subject should give their assent to participate, sign and date the written informed consent or a separate assent form. If the person objects to participating, this objection should be heeded.

Both investigators and IRB members must be aware that for some subjects, their decision-making capacity may fluctuate. For subjects with fluctuating decision making capacity or those with decreasing capacity to give consent, a re-consenting process with surrogate consent may be necessary. Although incompetent to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may subjects be forced or coerced to participate.

6.10.1 Consent by a Patient Representative

The regulations generally require that the investigator obtain informed consent from subjects. Under appropriate conditions, investigators also may obtain informed consent from a *legally authorized representative* of a subject.

Legally authorized representative means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research [45 CFR 46.102(c)]. Consent may be obtained from a court appointed guardian of the person **or** a health care agent appointed by the person in a Health Care Proxy or similar document that complies with the requirements of Massachusetts law, (M.G.L., Chapter 201D, including a durable power of attorney for health care. In the absence of a guardian or Health Care Agent, consult BH [Clinical Operations Policy](#) CO 9.100, Informed Consent and Health Care Decisions. Special rules apply when a potential subject is under the care or custody of a state agency.

This policy is designed to protect human subjects from exploitation and harm and, at the same time, make it possible to conduct essential research on problems that are unique to persons who are incompetent, or who have an impaired decision-making capacity.

The IRB will consult with legal counsel when necessary.

7 FDA-Regulated Research

FDA regulations apply to any research that involves a *test article* in a *clinical investigation* involving *human subjects* as defined by the FDA regulations. For FDA-regulated research, the IRB must apply the FDA regulations at 21 CFR 50 and 21 CFR 56, as well as, where appropriate, 45 CFR 46.

Use of investigational drugs must be conducted according to FDA IND regulations, 21 CFR Part 312, and other applicable FDA regulations. Use of an investigational device in a clinical trial to obtain safety and effectiveness data must be conducted according to FDA's IDE regulations, 21 CFR Part 812, and other applicable FDA regulations.

The following procedures describe the review and conduct of FDA-regulated research conducted under the auspices of BH.

7.1 Definitions

Investigational Drug An investigational drug for clinical research use is one for which the PI or a sponsor has filed an IND application (21 CFR Part 312) or an approved drug that is being studied for an unapproved or approved use in a controlled, randomized, or blinded clinical trial.

Investigational Device is a medical device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. As further stated, a device is any healthcare product that does not achieve its primary intended purpose by chemical action or by being metabolized.

IND IND means an investigational new drug application in accordance with 21 CFR Part 312.

IDE IDE means an investigational device exemption in accordance with 21 CFR 812.

Emergency Use Emergency use is defined as the use of an investigational drug or biological product with a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

Significant Risk (SR). A significant risk device means an investigational device that:

- (1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- (2) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- (3) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or

(4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Non-Significant Risk (NSR). A non-significant risk device is an investigational device other than a significant risk device.

Humanitarian Use Device (HUD). A Humanitarian Use Device is a device intended to benefit patients by treating or diagnosing a disease that affects fewer than 4,000 individuals in the United States per year.

7.2 FDA Exemptions

The following categories of clinical investigations are exempt from the requirements of FDA regulations for IRB review:

1. Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review. [21 CFR §56.104(c)]
2. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. [21 CFR §56.104(d)]

7.3 Investigational Drugs and Devices in Research

7.3.1 Massachusetts Law – Controlled Substances Registration

Massachusetts law (Chapter 94C, Section 8) requires the registration of investigators who use investigational and Schedule II drugs in research protocols. The law requires that any investigator who is using either an investigational drug, as defined by FDA regulations, or a Schedule II drug as part of a research protocol must register and obtain a license as a researcher from the Commonwealth of Massachusetts.

To facilitate compliance with the law, the State has determined that Department Chairs may opt to assume responsibility for the registration of research investigators within their departments. Investigators must verify that their Department Chair holds current registration that covers their research and maintain a copy of the license with the regulatory documentation for applicable protocols. In the absence of registration by the Department Chair, the investigator must register him/herself. In addition to the information required for the license, the State requires a current copy of the Department Chair's Massachusetts Medical License, Massachusetts Controlled Substance Practitioner Registration (if any), and the Drug Enforcement Administration Controlled Substance Registration. The license is renewed annually.

7.3.2 IND/IDE Requirements

The PI must indicate on the IRB application whether the research involves investigational drugs or devices. If so, the PI must indicate if there is an IND/IDE for the research and provide documented assurance from the sponsor that the manufacture and formulation of investigational or unlicensed test articles conform to federal regulations. Documentation of the IND/IDE could be a:

1. Industry sponsored protocol with IND/IDE.
2. Letter from FDA.
3. Letter from industry sponsor.
4. Other document and/or communication verifying the IND/IDE.

For investigational devices, NSR device studies follow abbreviated IDE requirements and do not have to have an IDE application approved by the FDA. If a sponsor has identified a study as NSR, then the investigator must provide an explanation of the determination. If the FDA has determined that the study is NSR, documentation of that determination must be provided.

If the research involves drugs or devices and there is no IND/IDE, the PI must provide a rationale why it is not required.

The IRB will review the application and determine:

1. Whether there is an IND/IDE and if so, whether there is appropriate supporting documentation.
2. If the research involves drugs or devices with no IND/IDE, and whether the research meets the criteria below.

7.3.3 IND Exemption

For drugs, an IND is not necessary if the research falls in one of the following categories:

1. The drug being used in the research is lawfully marketed in the United States and all of the following requirements are met:
 - a. The research is not intended to be reported to FDA in support of a new indication for use or to support any other significant change in the labeling for the drug
 - b. The research is not intended to support a significant change in the advertising for the product;

- c. The research does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product
 - d. The research is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively]
 - e. The research is conducted in compliance with the requirements concerning the promotion and sale of drugs [21 CFR 312.7]
 - f. The research does not intend to invoke FDA regulations for planned emergency research [21 CFR 50.24].
- 2. The research only involves one or more of the following: (a) Blood grouping serum, (b) Reagent red blood cells or (c) Anti-human globulin;
 - 3. For clinical investigations involving an in vitro diagnostic biological product, an IND is not necessary if a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and b) it is shipped in compliance with 312.160.
 - 4. A clinical investigation involving the use of a placebo is exempt from the requirements of this part if the investigation does not otherwise require submission of an IND.

7.3.4 Exempted IDE Investigations

For devices, an IDE is not necessary if:

- 1. The research involves a device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time ;
- 2. The research involves a device other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of 21 CFR 807 in determining substantial equivalence;
- 3. The research involves a diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:
 - a. Is noninvasive,
 - b. Does not require an invasive sampling procedure that presents significant risk,

- c. Does not by design or intention introduce energy into a subject, and
 - d. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure;
- 4. The research involves a device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk;
- 5. The research involves a device intended solely for veterinary use;
- 6. The research involves a device shipped solely for research on/or with laboratory animals and labeled in accordance with 21 CFR 812.5(c);
- 7. The research involves a custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

7.4 Responsibilities

7.4.1 PI

- 1. The PI is responsible for ensuring that the research is conducted according to all regulatory guidelines (See **Guidance on Special Considerations for the Oversight of Research Protocols using an FDA-regulated Product**) and BH policies and procedures.
- 2. For research involving investigational drugs: The PI is responsible for developing a plan for investigational drug accountability including storage, security, dispensing, administration, return, disposition, and records of accountability. The PI may delegate the responsibility for drugs/biologics accountability to the Investigational Drug Service or follow the guidelines established by the Investigational Drug Service and a SOP approved by the HRPP.
- 3. For research involving investigational devices:
 - a. The PI is responsible for developing a plan for investigational device accountability including storage, security, dispensing, administration, return, disposition, and records of accountability. This plan must be reviewed and approved by the IRB and may require additional sign off and review by the Safety Committee depending on the nature of the device. All devices received for a study must be stored in a locked environment under secure control with limited access. The area must be within an area of PI's control. Proper instructions on the use of the device must be provided to the subjects when applicable. A log must be kept regarding the receipt, use, and/or dispensing of the device and the disposition of remaining devices at the conclusion of the investigation.

- b. If a device is considered NSR by the PI or sponsor, but after review the IRB determines the device to have significant risk, upon receipt of written notice the PI is responsible for notifying the sponsor of the IRB's determination. The PI must provide the IRB with confirmation of this action.
 - c. The PI will submit to the sponsor and to the IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.
- 4. When a PI files an IND or IDE, the PI is considered the sponsor and as such is accountable for all of the FDA regulatory responsibilities and reporting obligations of both the PI and the sponsor, as described in the FDA regulations. The Research Plan asks the PI if he/she also acts as the sponsor of the research and, if so, asks him/her to affirm that he/she has reviewed the **Guidance Document on Requirements of the Sponsor and the Investigator as a Sponsor** and will comply with the regulatory responsibilities of a sponsor. The HRPP will provide education for investigators holding an IND or IDE on the sponsor regulations and periodically conduct random audits of PIs holding an IND or IDE via QA/QI reviews.

7.4.2 IRB

- 1. The IRB will review the research in accordance with the following requirements and the same criteria it would use in considering approval of any research involving an FDA-regulated product (21 CFR 56.111).
- 2. For research involving investigational devices:
 - a. Unless the FDA has already made a risk determination for the study, the IRB will review NSR studies and determine if the device represents significant or non-significant risk and report the findings to the PI in writing. The IRB will consider the risks and benefits of the medical device compared to the risks and benefits of alternative devices or procedures. Non-significant risk device studies do not require submission of an IDE application but must be conducted in accordance with the abbreviated requirements of IDE regulations.
 - b. Abbreviated IDE requirements:
 - a. The device is not a banned device.
 - b. The sponsor labels the device in accordance with 21 CFR 812.5.
 - c. The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device was not a significant risk device, and maintains such approval.

- d. The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, consent under 21 CFR 50 and documents it, unless documentation was waived.
 - e. The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations.
 - f. The sponsor maintains the records required under 21 CFR 812.140(b)(4) and (5) and makes the reports required under 21 CFR 812.150 (b)(1) through (3) and (5) through (10).
 - g. The sponsor ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 812.150(a)(1), (2), (5) and (7).
 - h. The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.
- c. If the study that has been submitted as NSR is considered SR, the IRB may approve the study, but the study cannot begin until an IDE is obtained.
 - d. The IRB will not review new protocol submissions involving significant risk devices under expedited review.
 - e. The IRB will document in the minutes and provide written documentation to the PI of the rationale for determining whether a device is classified as NSR/SR.
 - f. If the FDA has already made the SR or NSR determination for the study, the agency's determination is final and the IRB does not need to make a risk determination.

7.5 Emergency Use and Expanded Use Studies

7.5.1 Emergency Exemption from Prospective IRB Approval

HHS regulations do not permit human subjects research activities to be started, even in an emergency, without prior IRB approval. When emergency medical care is initiated without prior IRB review and approval, the patient may not be considered a research subject under 45 CFR Part 46. However, nothing in the HHS regulations at 45 CFR Part 46 is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable Federal, State or local law.

FDA defines emergency use as the use of an investigational drug or biological product with a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is no sufficient time to obtain IRB approval. If all conditions described in 21 CFR 56.102(d) exist then the emergency exemption from prospective IRB approval found at 21 CFR 56.104(c) may be utilized.

Informed consent must be obtained in accordance with and to the extent required by 21 CFR 50. Informed consent must be documented in writing in accordance with and to the extent required by 21 CFR 50.27.

The investigator should attempt to contact the IRB in advance of the emergency use whenever possible. The IRB must be notified within 5 working days when an emergency exemption is used. The Investigator must submit a completed “Emergency Use Report” form, and, when applicable, a copy of the patient consent form and the protocol for the IRB Chair or designee’s review within 5 days of the emergency use. This notification must not be construed as an approval for the emergency use by the IRB. The IRB Chair or designee will review the report to verify that circumstances of the emergency use conformed to FDA regulations. Documentation of the exemption will comprise the Investigator’s completed request form and written acknowledgment for the IRB. It is preferable for these forms to be received by the Chair of the IRB and acknowledged prior to commencing treatment.

Any subsequent use of the test article at the institution is subject to prospective IRB review.

7.5.1.1 Emergency Uses: Waiver of Informed Consent

An exception under FDA regulations at 21 CFR 50.23 permits the emergency use of an investigational drug, device, or biologic without informed consent where the investigator and an independent physician who is not otherwise participating in the clinical investigation certify in writing all four of the following specific conditions:

- a. The subject is confronted by a life-threatening situation necessitating the use of the test article;
- b. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
- c. Time is not sufficient to obtain consent from the subject’s legally authorized representative;
- d. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject’s life.

If time is not sufficient to obtain the independent physician determination before use of the test article, the actions of the investigator must be reviewed and evaluated in writing by an independent physician within 5 working days. The IRB must be notified within 5 working days when an emergency waiver is used. This notification must not be construed as an approval for the emergency waiver by the IRB. The IRB Chair or designee will review the report to verify that circumstances of the emergency waiver conformed to FDA regulations.

7.5.2 Expanded Access of Investigational Drugs

FDA regulations allow certain individuals not enrolled in clinical trials to obtain expanded access to investigational drugs, agents, or biologics through the following methods:

1. **Compassionate Use:** The term “compassionate use” is erroneously used to refer to the provision of investigational drugs outside of an ongoing clinical trial to a limited number of patients who are desperately ill and for whom no standard alternative therapies are available. The term “compassionate use” does not, however, appear in FDA or HHS regulations. It is preferable, instead, to use the names of the specific access programs when discussing the use of investigational articles outside of formal clinical trials.
2. **Group C Treatment Investigational New Drug (IND):** A means for the distribution of investigational drugs, agents, or biologics to oncologists for the treatment of cancer under protocols outside controlled clinical trials. Group C drugs, agents, or biologics usually have shown evidence of relative and reproducible efficacy in a specific tumor type. Although the FDA typically grants a waiver for most drugs used in Group C Treatment IND protocols, the BH IRB requires prospective IRB review and approval unless the use meets the criteria for Emergency Use as described above.
3. **Open – Label Protocol:** A study designed to obtain additional safety data, typically done when the controlled trial has ended and treatment continues. The purpose of such a study is to allow subjects to continue to receive the benefits of the investigational drug, agent, or biologic until marketing approval is obtained. Prospective IRB review and approval is required unless the use meets the criteria for Emergency Use as described above.
4. **Parallel Track:** A method approved by the FDA that expands the availability of investigational drugs, agents, or biologics as quickly as possible to persons with AIDS and other HIV-related diseases. These drugs, agents or biologics are utilized in separate protocols that “parallel” the controlled clinical trials and are essential to establish the safety and effectiveness of these new drugs, agents, or biologics. Although the Secretary of the Department of Health and Human Services may, on a protocol-by-protocol basis, waive the provisions of 45 CFR Part 46 where adequate protections are provided through other mechanisms, prospective IRB review and approval is required by the BH IRB unless the use meets the criteria for Emergency Use as described above.
5. **Treatment IND or Biologics:** A mechanism for providing eligible subjects with investigational drugs (as early in the drug development process as possible) for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. The FDA defines an immediately life-threatening disease as a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. The FDA will permit an investigational drug to be used under a treatment IND after sufficient data have been collected to show that the drug “may be effective” and does not have

- a. There are four requirements that must be met before a treatment IND can be issued:
 - i. The drug is intended to treat a serious or immediately life-threatening disease;
 - ii. There is no satisfactory alternative treatment available;
 - iii. The drug is already under investigation or trials have been completed; and
 - iv. The trial sponsor is actively pursuing marketing approval.
 - b. The FDA identifies two special considerations when a patient is to be treated under a Treatment IND:
 - i. Informed Consent. Informed consent is especially important in treatment use situations because the subjects are desperately ill and particularly vulnerable. They will be receiving medications which have not been proven either safe or effective in a clinical setting. Both the setting and their desperation may work against their ability to make an informed assessment of the risk involved. Therefore, the IRB should ensure that potential subjects are fully aware of the risks involved in participation.
 - ii. Charging for Treatment INDs. The FDA permits charging for the drug, agent, or biologic when used in a Treatment IND. Therefore, the IRB Committee should pay particular attention to Treatment INDs in which the subjects will be charged for the cost of the drugs. If subjects will be charged for use of the test article, economically disadvantaged persons will likely be excluded from participation. Charging for participation may preclude economically disadvantaged persons as a class from receiving access to test articles. The IRB should balance this interest against the possibility that unless the sponsor can charge for the drug, it will not be available for treatment use until it receives full FDA approval.
6. Single-Patient Use: The use of an investigational drug outside of a controlled clinical trial for a patient, usually in a desperate situation, who is unresponsive to other therapies or in a situation where no approved or generally recognized treatment is available. There is usually little evidence that the proposed therapy is useful, but may be plausible on theoretical grounds or anecdotes of success. Access to investigational drugs for use by a

7. Emergency IND: The emergency use of an unapproved investigational drug, agent, or biologic requires an emergency IND. The FDA has established mechanisms and guidance for obtaining an Emergency IND for the use of investigational drugs, agents, or biologics.
8. Emergency Waiver of IND: FDA regulations at 21 CFR 312.34, 312.35, and 312.36 address the need for an investigational drug to be used in an emergency situation that does not allow time for submission of an IND. The FDA may authorize shipment of the drug for a specific use in such a circumstance in advance of submission of an IND. Prospective IRB review is required unless the conditions for exemption are met (21 CFR 56.104(c) and 56.102(d)). Informed consent is required unless the conditions for exemption are met (21 CFR 50.23). All applicable regulations must be met including those at 21 CFR Parts 50 and 56, and 21 CFR 312.34 and 312.35.

7.5.3 Expanded Access of Investigational Devices

1. Compassionate Use (or Single Patient/Small Group Access). The compassionate use provision allows access for patients who do not meet the requirements for inclusion in the clinical investigation but for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition. This provision is typically approved for individual patients but may be approved to treat a small group. It must be a serious disease or condition and no alternative treatment available. Prior FDA approval is needed before compassionate use occurs.
2. Treatment Use. An approved IDE specifies the maximum number of clinical sites and the maximum number of human subjects that may be enrolled in the study. During the course of the clinical trial, if the data suggests that the device is effective, then the trial may be expanded to include additional patients with life-threatening or serious diseases. The criteria include:
 - a. Life-threatening or serious disease
 - b. No alternative
 - c. Controlled clinical trial
 - d. Sponsor pursuing marketing approval
3. Continued Access. FDA may allow continued enrollment of subjects after the controlled clinical trial under an IDE has been completed in order to allow access to the investigational medical device while the marketing application is being prepared by the sponsor or reviewed by FDA. There must a public health need or preliminary evidence that the device will be effective and there are no significant safety concerns.

7.6 Humanitarian Use Devices (HUD)

In accordance with 21 CFR 814.124, treatment with a HUD is subject to convened board initial review by the IRB. Expedited review procedures are acceptable for subsequent continuing reviews. At the time of review, the IRB will determine if written consent from participants for use of the HUD is necessary. It is the responsibility of the investigator to notify the sponsor if the IRB were ever to withdraw approval for use of a HUD. The sponsor should be notified within five days of notification of the withdrawal of approval. The sponsor is responsible for notification to the FDA if necessary. Investigators are reminded that Humanitarian Device Exemptions are for clinical use only and HUDs can be used only for the purposes outlined in the approved IRB application.

If a physician in an emergency situation determines that IRB approval for the use of the HUD at the facility cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be used without prior IRB approval. The procedures described under 7.5 must be followed including independent physician verification and the completion and submission to the IRB of the **Emergency Use Report** within five business days.

7.7 Waiver of Informed Consent for Planned Emergency Research

The conduct of planned research in life-threatening emergencies where the requirement to obtain prospective informed consent has been waived is covered by 21 CFR §50.24. The research plan must be approved in advance by the FDA or DHHS and the IRB, and publicly disclosed to the community in which the research will be conducted. Such studies are not allowed under the regulations covering the emergency use of a test article in a life-threatening situation (21 CFR §56.104(c)).

BH does not currently intend to conduct such research. Should planned emergency research be proposed, appropriate policies and procedures will be developed and implemented.

8 Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events

BH complies with DHHS and FDA regulations which state that institutions must have written policies on reporting unanticipated problems involving risks to subjects or others to the IRB, institutional officials and relevant federal agencies and departments.

The following procedures describe how unanticipated problems involving risk to subjects or others are handled in research under the auspices of BH. Unless specifically required by the IRB, the BH IRB does not accept reports of adverse events that do not meet the definition of an Unanticipated Problem Involving Risks to Subjects or Others. Per federal regulation, Unanticipated Adverse Device Events must be reported to the sponsor and the reviewing IRB as soon as possible, but in no event later than 10 working days after the investigator first learns of the event [21 CFR 812.150(a)(1)].

8.1 Definitions

Unanticipated problems involving risk to participants or others. Unanticipated problems involving risks to participants or others refer to any incident, experience, outcome, or new information that::

1. Is unexpected,
2. Is related or possibly related to participation in the research, and
3. Indicates that subjects or others are at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Unexpected. The incident, experience or outcome is not expected (in terms of nature, severity, or frequency) given the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and consent documents; and the characteristics of the subject population being studied;

Related There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.

Adverse Event An Adverse Event (AE) is defined as any untoward physical or psychological occurrence in a human subject participating in research. An AE can be any unfavorable or unintended event including abnormal laboratory finding, symptom or disease associated with the research or the use of a medical investigational test article.

Serious Adverse Event A Serious Adverse Event (SAE) is defined as death; a life threatening experience; hospitalization (for a person not already hospitalized); prolongation of hospitalization (for a patient already hospitalized); persistent or significant disability or

incapacity; congenital anomaly and/or birth defects; or an event that jeopardizes the subject and may require medical or surgical treatment to prevent one of the preceding outcomes.

Unexpected Adverse Device Effect. An Unexpected Adverse Device Effect (UADE) means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that related to the rights, safety, or welfare of subjects [21 CFR 812.3(s)].

8.2 Procedures

8.2.1 Reporting

Investigators must report possible UAPs and UADEs to the sponsor, if applicable, and the IRB as soon as possible, but in no event later than 10 working days after the investigator first learns of the event.

Investigators must promptly report the following problems to the IRB:

- 1) Adverse events involving direct harm to participants which in the opinion of the principal investigator meet the criteria for an unanticipated problem involving risk to subjects or others.
- 2) Unanticipated Adverse Device Effects (UADE)
- 3) An unanticipated event related to the research that exposes participants to potential risk but that does not involve direct harm to participants.
- 4) An unanticipated event related to the research that exposes individuals other than the research participants (e.g., investigators, research assistants, students, the public, etc.) to potential risk.
- 5) IND Safety Reports from sponsors that meet the criteria for an unanticipated problem involving risk to subjects or others.
- 6) New information that indicates a change to the risks or potential benefits of the research. For example:
 - a) An interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different than initially presented to the IRB.
 - b) A paper is published from another study that shows that the risks or potential benefits of the research may be different than initially presented to the IRB.
- 7) A breach of confidentiality.

- 8) Incarceration of a participant in a protocol not approved to enroll prisoners.
- 9) Changes increasing the risk to subjects and/or affecting significantly the conduct of the trial.
- 10) Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant.
- 11) Complaint of a participant when the complaint indicates unexpected risks or cannot be resolved by the research team.
- 12) Protocol deviation (meaning an accidental or unintentional change to the IRB approved protocol) that harmed participants or others or that indicates participants or others may be at increased risk of harm.
- 13) Sponsor imposed suspension for risk.
- 14) Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
- 15) Any other event that indicates participant or others might be at risk of serious, unanticipated harms that are reasonably related to the research.

8.2.2 Submission of Reports

Investigators or the study team must report possible unanticipated problems to the IRB using the **Report of an Unanticipated Problem** form. Reports that do not potentially meet the definition of Unanticipated Problem should come in as an **“Other Reportable Event”**. The report should contain the following:

1. Detailed information about the possible unanticipated problems, including relevant dates.
2. Any corrective action, planned or already taken, to ensure that the possible unanticipated problems is corrected and will not occur again.
3. An assessment of whether any subjects or others were placed at risk as a result of the event or suffered any physical, social, or psychological harm and any plan to address these consequences.
4. Any other relevant information.
5. Any other information requested by the HRPP or IRB.

A report of a possible unanticipated problem involving risks to participants or others will be immediately forwarded by IRB staff to the HRPP Director and IRB Chair or designee if the IRB

staff believes that immediate intervention may be required to protect participants or others from serious harm.

Upon receipt of a report of a possible unanticipated problem from someone other than the investigator or study staff, the HRPP Director or IRB Chair will notify the PI on the study when appropriate.

8.2.3 IRB Procedures for Handling Reports of Possible Unanticipated Problems

8.2.3.1 Review by IRB Staff and Chair

1. Upon receipt of an Unanticipated Problem Report from a Principal Investigator, the IRB staff checks the form for completeness. If any applicable sections of the form are incomplete or have been answered unsatisfactorily, the IRB staff will contact the investigator or the designated contact person to obtain additional information.
2. The IRB Chair and/or other experienced member(s) designated by the IRB chairperson receive and reviews the report of the event(s) considered to be an unanticipated problem. The IRB chairperson (or designee) will make the final determination as to whether the event is to be regarded as an unanticipated problem.
3. Based on the information received from the investigator, the IRB Chair or designee may suspend research to ensure protection of the rights and welfare of participants. Suspension directives made by the IRB Chair or designee must be reported to a meeting of the convened IRB.
4. The IRB or the IRB Chair (or designee) has authority to require submission of more detailed contextual information by the PI, the sponsor, the study coordinating center, or DSMB/DMC about any event occurring in a research protocol as a condition of the continuation of the IRB's approval of the research.
5. If the reviewer determines that the reported problem does not meet the definition of an UAP this determination is documented within the "Reviewer's Comments" section of IRBNet, the determination is communicated to the investigator, and no further action is taken.
6. If the reviewer considers that the problem is an unanticipated problem, but that the risk is no more than minimal, the reviewer will review:
 1. The currently approved protocol
 2. The currently approved consent document
 3. Previous reports of unanticipated problems involving risks to participants or others

4. The investigator's brochure, if one exists

After reviewing all of the materials, the reviewer will take appropriate action depending on the nature of the risk involved, including modification of the protocol or the consent form, if applicable. The results of the review will be recorded in IRBNet, communicated to the investigator, and reported to the IRB. As applicable, events determined to be unanticipated problems will be reported to the relevant regulatory agencies and institutional officials according to the procedures in Section 12.

7. All reported unanticipated problems where the risk is more than minimal will be reviewed at a convened IRB meeting.

8.2.3.2 Convened IRB Review

The primary reviewer and all IRB members will have electronic access to the protocol file including the event report, the currently approved consent document, previous reports of unanticipated problems involving risks to participants or others, the investigator's brochure (if one exists), and recommendations from the IRB Chair or designee, when appropriate.

After review of the protocol file and event report, the convened IRB will make findings and recommendations based on the following considerations:

1. Whether the reported event is an unanticipated problem involving risks to participants or others according to the definition in this policy.
2. What action in response to the report is appropriate.
3. Whether suspension or termination of approval is warranted.

If the IRB finds that the event is not an unanticipated problem involving risks to participants or others, according to the definition in the policy, the IRB may recommend any of the following actions:

1. No action
2. Requiring modifications to the protocol
3. Revising the continuing review timetable
4. Modifying the consent process
5. Modifying the consent document
6. Providing additional information to current participants (e.g. whenever the information may relate to the participant's willingness to continue participation)

7. Providing additional information to past participants
8. Requiring additional training of the investigator and/or study staff
9. Other actions appropriate for the local context

If the IRB finds that the event is an unanticipated problem involving risks to participants or others, according to the definition in the policy, the IRB may recommend any of the following actions:

1. Requiring modifications to the protocol
2. Revising the continuing review timetable
3. Modifying the consent process
4. Modifying the consent document
5. Providing additional information to current participants (e.g. whenever the information may relate to the participant's willingness to continue participation)
6. Providing additional information to past participants
7. Requiring additional training of the investigator and/or study staff
8. Reconsidering approval
9. Requirement that current participants re-consent to participation
10. Monitoring of the research
11. Monitoring of the consent
12. Referral to other organizational entities (e.g., legal counsel, risk management, institutional official)
13. Suspending the research
14. Terminating the research
15. Other actions appropriate for the local context

If a report suggests that participant safety is at risk, the IRB may immediately suspend or terminate the research. Any suspension or termination of research by the IRB must be promptly reported to the IO and OHRP (if federally-funded), and FDA (if FDA-regulated research) through the IO. This should be done in writing.

If, after reviewing a report, the IRB finds that the event is an unanticipated problem involving risks to participants *or* others or that suspension or termination of approval is warranted, the IRB will:

1. Notify the investigator in writing of its findings, with copies to the Department Chair or equivalent of the investigator's department, other affected units, other parties within the institution as applicable (i.e., the Research Integrity Officer, Risk Management, Corporate Compliance), and
2. Report its findings and recommendations to the Institutional Official for further reporting to the appropriate federal officials (OHRP and FDA) and sponsor, as applicable.
3. Investigators can request the IRB reconsider its determination as described in Section 13.4.

9 Protocol Exceptions or Deviations

It is the policy of the BH IRB to be notified of all protocol deviations or exceptions.

The following procedures describe how protocol deviations and exceptions are reported to the IRB

9.1 Definitions

Exceptions Protocol exceptions are defined as circumstances in which the specific procedures called for in a protocol are not in the best interests of a specific patient/subject (example: patient/subject is allergic to one of the medications provided as supportive care). Usually it is a deviation that is anticipated and happens with prior agreement from the sponsor.

Deviations A protocol deviation is defined as a deviation from the approved research activity without prior approval of the IRB (protocol visit scheduled outside protocol window, blood work drawn outside protocol window, required procedure omitted, etc.). The IRB will review these reports for frequency and may audit any protocol reporting frequent deviations.

9.2 Exceptions

It is the responsibility of the Investigator to seek approval of the IRB any proposed exceptions to be made to the protocol. The IRB will perform an expedited review of the **Modification Request** form submitted by the Investigator along with documentation of Sponsor justification and approval.

These exceptions must be approved by the sponsor and IRB before being implemented.

Exceptions may not increase risk or decrease benefit, affect the participant's rights, safety, welfare, or affect the integrity of the resultant data.

9.3 Deviations

It is the responsibility of the Investigator not to deviate from the research activity approved by the IRB, except to avoid an immediate hazard to the participant. The Investigator must submit a **Modification Request** to the IRB and receive written approval prior to implementation of any change.

Deviations that increase risk have potential to recur or are undertaken to eliminate an immediate hazard would be considered an Unanticipated Problem and should be handled according to Section 8.

Deviations from the approved research activity without IRB approval must be submitted to the IRB via a **Protocol Deviation Report**.

Repetitive deviations may be ruled by the IRB to constitute non-compliance.

9.4 Reporting & Review

Protocol Deviation Reports are to be submitted to the IRB for those events that qualify as a protocol deviation. The IRB staff will forward the report to the IRB Chair or designee for review. An acknowledgment will be sent back to the investigator for the study file.

Upon receipt of the report, the Chair or designee will make a preliminary assessment as to whether the incident warrants immediate suspension of the research project. If a suspension is warranted, the procedures in Section 3.9 will be followed.

The Chair or designee will make an assessment as to any appropriate corrective action and whether a modification of the protocol or consent form is warranted. If the incident meets the definition of non-compliance, it will be considered an allegation of non-compliance according to Section 11. If the incident meets the definition of an unanticipated problem involving risk to subjects or others, it will be handled according to Section 8.

The Chair may choose to place any deviation or exception on the agenda of the next convened IRB meeting for discussion. The investigator may be asked to appear at that meeting to answer any questions or clarify issues for the IRB.

10 Complaints or Concerns

Complaints or concerns may be received in the HRPP or IRB office via mail, e-mail, FAX, telephone, the “Suggestions or Concerns” submission links on the internal and external website, or forwarded from the Corporate Compliance hot line. All complaints, written or verbal, and regardless of point of origin are forwarded to the Director or, in the absence of the Directors, to the IRB Chair. Complainants may choose to remain anonymous.

The Director in collaboration with the Chair of the IRB or designee will promptly handle (or delegate staff to handle), and, if necessary, investigate all complaints, concerns, and appeals received by the IRB. This includes complaints, concerns, and appeals from investigators, research participants, and others.

Upon receipt of the complaint or concern, the Director or Chair will make a preliminary assessment whether the complaint warrants immediate suspension of the research project. If a suspension is warranted, the procedures in Section 3.9 will be followed.

If the complaint or concern meets the definition of non-compliance, it will be considered an allegation of non-compliance according to Section 11.

If the complaint or concern meets the definition of an unanticipated problem involving risk to subjects or others, it will be handled according to Section 8.

If the complaint or concern is indicative of possible scientific misconduct, the Research Integrity Officer will be immediately notified.

If the complaint is not submitted anonymously, the Director or Chair shall generate a responsive letter or e-mail within 3 business days of receipt of the complaint or concern to acknowledge receipt and investigation.

11 Non-compliance

As part of its commitment to protecting the rights and welfare of human subjects in research, BH reviews all allegations of non-compliance and takes any necessary action to ensure the ethical conduct of research.

The following procedures describe how allegations of non-compliance are handled by the IRB.

11.1 Definitions

Non-compliance Non-compliance is defined as failure to comply with any of the regulations and policies described in this document and failure to follow the determinations of the IRB. Non-compliance may be minor or sporadic or it may be serious or continuing.

Serious non-compliance Serious non-compliance is defined as failure to follow any of the regulations and policies described in this document or failure to follow the determinations of the IRB and which, in the judgment of either the convened IRB, increases risks to participants, decreases potential benefits, or compromises the integrity of the Human Research Protection Program. Research being conducted without prior IRB approval is considered serious noncompliance.

Continuing non-compliance Continuing non-compliance is defined as a pattern of non-compliance that, in the judgment of the convened IRB, suggests a likelihood that instances of non-compliance will continue without intervention. Continuing non-compliance also includes failure to respond to a request to resolve an episode of non-compliance.

Allegation of Non-Compliance Allegation of Non-Compliance is defined as an unproved assertion of non-compliance.

Finding of Non-Compliance Finding of Non-Compliance is defined as an allegation of non-compliance that is proven true or a report of non-compliance that is clearly true. (For example, a finding on an audit of an unsigned consent document, or an admission of an investigator that the protocol was willfully not followed would represent reports of non-compliance that would require no further action to determine their truth and would therefore represent findings of non-compliance.) Once a finding of non-compliance is reached, it must be categorized as serious, non-serious, or continuing.

11.2 Non-compliance

Investigators and their study staff are required to report instances of possible non-compliance. The Principal Investigator is responsible for reporting any possible non-compliance by study personnel to the IRB. Common reports to the IRB that are not serious or continuing are typically protocol deviations. However, any individual or employee may report observed or apparent instances of noncompliance to the IRB. In such cases, the reporting party is responsible for making these reports in good faith, maintaining confidentiality and cooperating with any IRB and/or institutional review of these reports.

If an individual, whether investigator, study staff or other, is uncertain whether there is cause to report noncompliance, he or she may contact the HRPP Director or IRB Chair directly to discuss the situation informally.

Reports of non-compliance must be submitted to the IRB within 10 working days of discovery of the noncompliance. The report must include a complete description of the noncompliance, the personnel involved and a description of any initiated or proposed corrective actions.

11.2.1 Review of Allegations of Non-compliance

All allegations of non-compliance will be reviewed by the HRPP Director in collaboration with the IRB Chair or designee, who will review all documents relevant to the allegation which may include:

1. the report of noncompliance,
2. the last approved IRB application and protocol, the last approved consent document,;
3. the grant, if applicable; and,
4. Any other pertinent information (e.g., questionnaires, DSMB reports, etc.).

The Director or Chair will review the allegation and make a determination as to the truthfulness of the allegation. They may request additional information or an audit of the research in question.

When it is determined that noncompliance did not occur because the incident was within the limits of an approved protocol for the research involved, the determination is reported in writing to the PI and if applicable the reporting party. The determination letter will be copied to the Institutional Official in cases where the Institutional Official and any other parties had been notified at the outset.

If in the judgment of the Director or Chair, the reported allegation of non-compliance is true, the non-compliance will be processed according to Section 11.2.2.

If in the judgment of the Director or Chair, any allegation or findings of non-compliance warrants suspension of the research before completion of any review or investigation to ensure protection of the rights and welfare of participants, the Director or Chair may suspend the research as described in Section 3.9 with subsequent review by the IRB.

If in the judgment of the Director or Chair, any allegation or finding of non-compliance may represent scientific misconduct, the Research Integrity Officer will be immediately notified.

The Director or Chair may determine that additional expertise or assistance is required to make these determinations and may form an ad hoc committee to assist with the review and fact gathering process. When an ad hoc committee assists in the review process, the Chair is responsible for assuring that minutes of the meeting are generated and kept to help support any determinations or findings made by the ad hoc committee.

11.2.2 Review of Findings of Non-compliance

Noncompliance is not serious or continuing:

When the Director or Chair determines that the noncompliance occurred, but the noncompliance does not meet definition of serious or continuing noncompliance, the determination is reported in writing to the PI and if applicable the reporting party. The Director and Chair will work with the PI to develop a corrective action plan to prevent future noncompliance. The report of noncompliance and corrective action is reported to the IRB through the “expedited review report”. If however, the PI refuses to cooperate with the corrective action plan, the matter is referred to a convened meeting of the IRB with notification to the IO.

Serious or Continuing Noncompliance

When the Director or Chair determines that noncompliance has occurred and that the noncompliance may meet the definition of serious or continuing noncompliance, the report of noncompliance is referred for review by the IRB at the next convened available meeting. However, the Director or Chair may use discretion and call an emergency IRB meeting should the circumstances warrant such an urgent meeting.

All findings of serious or continuing non-compliance referred to the IRB will be reviewed at a convened meeting. All IRB members will have electronic access to the project file and will be provided with all documents relevant to the allegation:

At this stage, the IRB may:

1. Find that there is no issue of non-compliance
2. Find that there is noncompliance that is neither serious nor continuing and an adequate corrective action plan is in place
3. Find that there is serious or continuing non-compliance and take actions as described under 11.2.4
4. Find that there may be serious or continuing non-compliance and direct that a formal inquiry (described below) be held; or
5. Request additional information.

11.2.3 Inquiry Procedures

A determination may be made by the IRB that an inquiry is necessary based on several issues that may include but are not limited to:

1. Subjects' complaint(s) that rights were violated;

2. Report(s) that investigator is not following the protocol as approved by the IRB;
3. Unusual and/or unexplained adverse events in a study;
4. Repeated failure of investigator to report required information to the IRB.

A subcommittee is appointed consisting of IRB members, non-members if appropriate, and HRPP/IRB Staff to ensure fairness and expertise. The subcommittee is given a charge by the IRB, which can include any or all of the following:

1. Review of protocol(s) in question;
2. Review of sponsor audit report of the investigator, if appropriate;
3. Review of any relevant documentation, including consent documents, case report forms, subject's investigational and/or medical files etc., as they relate to the investigator's execution of her/his study involving human subjects;
4. Interview of appropriate personnel if necessary;
5. Preparation of either a written or oral report of the findings, which is presented to the full IRB at its next meeting;
6. Recommend actions if appropriate.

11.2.4 Final Review

The results of the review or inquiry will be reviewed at a convened IRB meeting where the IRB will receive a report. If the results of the review or inquiry substantiate the finding of serious or continuing non-compliance, the IRB's possible actions could include, but are not limited to:

1. Require a correction action plan either from the investigator or as developed by the IRB
2. Verification that participant selection is appropriate and observation of the actual informed consent
3. An increase in data and safety monitoring of the research activity
4. Require a directed review of targeted areas of concern
5. Require a status report after each participant receives intervention
6. Modify the continuing review cycle
7. Require additional Investigator and staff education
8. Notify current subjects, if the information about the non-compliance might affect their

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

In cases where the IRB determines that the event of noncompliance also meets the definition of an unanticipated problem involving risks to subjects or others, the policy and procedure for review of such events will also be followed.

The investigator and their Chair or equivalent is informed of the IRB determination and the basis for the determination in writing. Investigators can request the IRB reconsider its determination as described in Section 13.4. If the IRB determines that the non-compliance was serious or continuing, the results of the final review will be reported as described below in Section 12.

12 Reporting to Regulatory Agencies and Institutional Officials

Federal regulations require prompt reporting to appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval. The BH HRPP will comply with this requirement and the following procedures describe how these reports are handled.

Note: Reporting to a regulatory agency is not required if the event occurred at a site that was not subject to the direct oversight of the organization, and the agency has been notified of the event by the investigator, sponsor, another organization, or other mechanism.

12.1 Procedures

The staff of the HRPP/IRB will initiate these procedures as soon as the IRB takes any of the following actions:

1. Determines that an event may be considered an unanticipated problem involving risks to participants or others
2. Determines that non-compliance was serious or continuing
3. Suspends or terminates approval of research

The Director or designee is responsible for preparing reports or letters which includes the following information:

1. The nature of the event (Unanticipated problem involving risks to participants or others, serious or continuing non-compliance, suspension or termination of approval of research)
2. Name of the institution conducting the research
3. Title of the research project and/or grant proposal in which the problem occurred
4. Name of the Principal Investigator on the protocol
5. Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement)
6. A detailed description of the problem including the findings of the organization and the reasons for the IRB's decision

7. Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.)
8. Plans, if any, to send a follow-up or final report by the earlier of
 - A specific date
 - When an investigation has been completed or a corrective action plan has been implemented

The RIO and the IO review and modify the report as needed. The Institutional Official is the signatory for all such correspondence from the institution.

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 that agency.

A copy of the report will be sent to the Research Integrity Officer, IRB Chair(s), the Principal Investigator and his/her Chair or Supervisor, the Medical Staff Office or Risk Management if reporting to a state regulatory agency is required by statute or regulation, the Sponsor or Contract Research Organization if required by contract, and others as deemed appropriate by the Institutional Official.

The Director ensures that all steps of this policy are completed within 30 working days of the determination. In cases where the IRB and IO determine that additional information is required before submitting a final report, a preliminary report may be made. For more serious actions, the Director will expedite reporting.

13 Investigator Responsibilities

Principal Investigators are ultimately responsible for the conduct of research. Principal Investigators may delegate research responsibility. However, investigators must maintain oversight and retain ultimate responsibility for the conduct of those to whom they delegate responsibility.

The following procedures describe the investigator responsibilities in the conduct of research involving human participants.

13.1 Investigators

13.1.1 Principal Investigators

The IRB recognizes one and only one Principal Investigator (PI) for each study. The PI has ultimate responsibility for all of the research activities related to the study.

At BH, individuals who serve as the Principal Investigator on a research project involving human subjects must have the appropriate expertise and experience, as generally demonstrated by a faculty appointment at the rank of Assistant Professor or higher and/or as a credentialed member of the medical staff or associate professional staff. Other individuals may serve as Principal Investigator with the approvals of the Department Chair or Vice President (if employed or credentialed by Baystate Medical Center), the Institutional Official, and the IRB. Principal Investigators for FDA-regulated clinical trials must be credentialed physicians on the medical staff in good standing and hold a current full license from the Board of Registration in Medicine in the Commonwealth of Massachusetts.

Students, residents, and fellows may not serve as a Principal Investigator but may serve as a sub-investigator. Chief Residents, who have completed their core residency training and are serving an additional year in the residency program, may serve as Principal Investigator if they are otherwise eligible and are approved by the Department Chair and Institutional Official.

Protocols that require expertise or skills beyond those held by the Principal Investigator must be modified to align with the investigator's expertise or skills, or have one or more additional qualified faculty as sub-investigator(s).

Principal Investigators are required to personally conduct or supervise the conduct of the research. Delegation of responsibilities to other individuals, and the qualifications and training of those individuals to fulfill those responsibilities, must be documented. In the event that a Principal Investigator anticipates an extended absence, such as for a sabbatical, arrangements must be made for either an investigator hold or for designation of a sub-investigator to serve as Principal Investigator for the duration of the absence. The designated sub-investigator must be qualified and thoroughly trained in the protocol. Such designations must be documented, reported to, and approved by the IRB. Principal Investigators who leave the institution are

required to either close the research project or to transfer responsibility for the project, with IRB approval, to a qualified Principal Investigator prior to their departure.

13.1.2 Research Team

The PI and other individuals, also known as key personnel, who contribute to the scientific development or execution of a project in a substantive, measurable way, whether or not they receive salaries or compensation under the protocol. The research team also consists of individuals who intervene or interact directly with human subjects, or who analyze data and/or tissue, for the purposes of the research. All individuals who directly interact or intervene with local subjects or their identifiable data and/or tissue for the purposes of the research must be included on the IRB submission. Individuals such as statisticians who may provide significant support to the research but do not have any direct interaction with local subjects or their identifiable data do not need to be included on the IRB submission unless specifically requested to evidence appropriate expertise/resources to conduct the research.

13.2 Responsibilities

In order to satisfy the requirements of this policy, investigators who conduct research involving human subjects must:

1. Develop and conduct research that is in accordance with the ethical principles in the Belmont Report
2. Develop a research plan that ensures that risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes;
3. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, include additional safeguards in the study to protect the rights and welfare of these subjects;
4. Maintain and adhere to HRPP-approved basic Standard Operating Procedures for Investigators. Template versions are available on eWorkplace and upon request from HRPP Integrity and Education staff;
5. Ensure that all research involving human subjects receives IRB review and approval in writing before commencement of the research. Seek HRPP or IRB assistance when in doubt about whether proposed research requires IRB review;
6. Have sufficient resources necessary to protect human subjects, including:
 - a) Access to a population that would allow recruitment of the required number of

- b) Sufficient time to conduct and complete the research.
 - c) Adequate numbers of qualified staff.
 - d) Adequate facilities.
 - e) A process to ensure that all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions.
 - f) Availability of medical or psychological resources that subjects might require as a consequence of the research.
7. Assure that all procedures in a study are performed with the appropriate level of supervision and only by individuals who are licensed or otherwise qualified to perform such under the laws of Massachusetts and the policies of BH;
 8. Assure that all key personnel are educated in the regulatory requirements regarding the conduct of research and the ethical principals upon which they are based;
 9. Ensure that pertinent laws, regulations, and institution policies and guidelines are observed by participating investigators and research staff;
 10. Protect the rights and welfare of prospective subjects;
 11. Recruit subjects in a fair and equitable manner
 12. Obtain and document informed consent as required by the IRB and ensure that no human subject is involved in the research prior to obtaining their consent unless the requirement has been waived by the IRB;
 13. Have plans to monitor the data collected for the safety of research subjects;
 14. Protect the privacy of subjects and maintain the confidentiality of data;
 15. Have a procedure to receive complaints or requests for additional information from subjects and respond appropriately,
 16. Ensure that modifications to approved research are not implemented prior to IRB review and approval except when necessary to eliminate apparent immediate hazards to subjects;
 17. Comply with all HRPP and IRB decisions, conditions, and requirements;
 18. Ensure that protocols receive timely continuing IRB review and approval;

19. Report unanticipated problems , noncompliance, and other reportable events to the IRB according the procedures detailed in this manual;
20. Maintain complete and accurate records of the research.

Principal Investigators are required to personally conduct or supervise the conduct of the research. Delegation of responsibilities to other individuals, and the qualifications and training of those individuals to fulfill those responsibilities, must be documented.

Screening of subjects for eligibility and the consent process are critical tasks crucial to the protection of human subjects. At BH, delegations of these tasks to students and professional research staff should be in accordance with the following guidelines. Direct involvement and/or monitoring of these tasks by the PI and appropriate sub-investigators is strongly encouraged. Refer to the Clinical Research Matrix (Career Ladders) on eWorkplace for additional information on level-based responsibilities for professional research staff. The IRB may grant exceptions to the guidelines for screening and consent on a case-by-case basis. Such requests should be submitted in writing via the IRB electronic system including a justification or rationale for the exception.

Study Type	Non-interventional studies		Interventional Studies	
Task:	Screening	Informed Consent	Screening	Informed Consent
CR Assistant I	No responsibility	No responsibility	No responsibility	No responsibility
CR Assistant II	May assist	May assist	May assist	No responsibility
CR Coordinator I (non-nurse)	May assist or conduct	May assist or conduct	May assist	May assist
CR Coordinator II (non-nurse)	May assist or conduct	May assist or conduct	May assist or conduct	May assist or conduct
Senior CR Coordinator (non-nurse)	May assist or conduct	May assist or conduct	May assist or conduct	May assist or conduct
Nurse Coordinator I	May assist or conduct	May assist or conduct	May assist or conduct	May assist or conduct
Nurse Coordinator II	May assist or conduct	May assist or conduct	May assist or conduct	May assist or conduct
Nurse Coordinator III	May assist or conduct	May assist or conduct	May assist or conduct	May assist or conduct
Nurse Coordinator IV	May assist or conduct	May assist or conduct	May assist or conduct	May assist or conduct

CR Manager I	May assist or conduct	May assist or conduct	May assist or conduct	May assist or conduct
CR Manager II	May assist or conduct	May assist or conduct	May assist or conduct	May assist or conduct
College students (undergraduate)*	May assist	May assist	No responsibility	No responsibility
Medical and other graduate students*	May assist or conduct	May assist or conduct	May assist	May assist
Associates in Research who are not enrolled in a degree-granting program*	May assist	May assist	No responsibility	No responsibility

*Post-high school students who are at BMC under an institutional or individual affiliation agreement or as an Associate in Research. High school-aged students may not participate in human subjects' research but may observe in accordance with the observership policy.

13.3 Training / Ongoing Education of Investigators and Research Team

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

13.3.1 Initial Education

The PI and key personnel must complete the BH Required Core Modules in CITI Course in the Protection of Human Research Subjects.

New research protocols and applications for continuing review will not be accepted from principal investigators where all key personnel have not completed the initial education requirement.

13.3.2 Waiver of BH Education Requirements

If external investigators or other members of the research team can verify that they have successfully completed human subjects research training equivalent to that required by BH, they may request a waiver of the BH specific requirements by contacting the HRPP Director.

13.3.3 Continuing Education and Recertification

All investigators and members of their research teams must complete continuing education every three (3) years after certification of Initial Education for as long as they are involved in human subject research. There is no exception to this requirement. Acceptable training includes completion of specified CITI refresher modules. Attendance at PRIM&R or OHRP seminars and conferences, attendance at selected HRPP Human Subjects Research Presentations, and other training may be acceptable. In these cases the researcher should check with the HRPP office for a determination.

Investigators must submit evidence of current education at initial and continuing review. New research protocols and applications for continuing review will not be accepted from principal investigators who have not submitted satisfactory evidence of education in human subjects protections.

Investigators who are also IRB members or HRPP/IRB staff will satisfy the training requirements for IRB members and staff described in this policy under Section 2.12.

Failure to meet this requirement will result in the administrative removal of the Investigator from all protocols on which the Investigator is listed, or suspension of the study if the Investigator is the Principal Investigator. Once removed, Investigators must not participate in any research activities until the training requirement has been met and the Investigators have been reinstated by the IRB. Reinstatement on each protocol can only be accomplished through the submission and approval of a **Modification Request** (amendment) to the IRB.

13.3.4 Professional Certification of Clinical Research Staff

Clinical research staff are required to achieve professional certification in clinical research within one year of eligibility. This policy applies to all BH Clinical Research Assistants, Coordinators, Nurse Coordinators, Regulatory Specialists, and Managers/Supervisors. Professional certification in clinical research is currently obtained through either the Society of Clinical Research Associates (SoCRA) or the Association for Clinical Research Professionals (ACRP). In addition, a limited number of colleges and universities offer equivalent certificate programs in clinical research.

Certification must be attained within one year of eligibility, or within one year of date of hire for those entering the system, who are already eligible. If the candidate fails to achieve certification on the first attempt, they will be granted a second attempt within one year. Failure on the second attempt will result in demotion to the levels of the matrix (Research Assistant 1 or 2, Research Nurse Coordinator 1) where certification is not a requirement.

The Division of Academic Affairs will provide financial reimbursement for the cost of the certification examination (first and second attempt), for re-certification fees, and for membership in the certifying organization if membership is required as a criterion for maintaining certification.

The Division of Academic Affairs hosts educational events to support clinical research staff in obtaining the continuing education credits necessary to maintain certification. Certification examination study materials and other resources are available through the Human Research Protections Program (HRPP).

13.3.5 Additional Resources

Human research protection information will be made available on the HRPP/IRB intranet pages on an ongoing basis to ensure that the research community is apprised of current regulatory and policy requirements and training opportunities.

13.4 Request for IRB Reconsideration

An investigator can request that the IRB reconsider any determination, whether it is related to a specific submission, a determination that an unanticipated problem has occurred, a finding of serious or continuing noncompliance, or a suspension or termination.

It is essential that requests for reconsideration be received in a timely manner. For determinations of non-compliance, unanticipated problems, or suspensions or terminations, requests for reconsideration should be submitted within ten (10) business days of receipt of the IRB determination so that the institution can fulfill its reporting obligations to external entities in a timely fashion. For requests related to an IRB requirement on a specific submission, requests for reconsideration should be submitted within thirty (30) days.

An investigator can request reconsideration by submitting a response package to the IRB via IRBNet. The submission package should include a memo specifying the exact request of the investigator, the basis for the request, and modified application form or other materials as applicable.

If the original determination was made by the convened board, the investigator's request will be considered at the next available meeting of the IRB. If the original determination was made by a reviewer under the expedited review process, the request for reconsideration will be given to the same reviewer whenever possible. The IRB will make a determination whether to uphold, reverse or modify its decision. The IRB notifies the investigator of the final outcome via a letter produced within IRBNet. For reconsiderations related to determinations of non-compliance, unanticipated problems, or suspensions or terminations, the IO, Department Chair or Supervisor, and other parties will be notified of the final outcome as applicable.

13.5 Investigator Concerns

Investigators who have concerns or suggestions regarding BH's Human Research Protection Program should convey them to the Director, Institutional Official, or other responsible parties (e.g. IRB Chair, Department Chair), who will in turn inform the Institutional Official. The issues will be reviewed, and when deemed necessary, the Institutional Official will convene the

appropriate parties to form a response for the investigator, make necessary procedural or policy modifications, or take other steps, as warranted.

It is essential that concerns are brought forward in a timely manner as it is very difficult to determine facts as time elapses. Reports of project specific concerns should include as much detail as possible including the name of the PI, the IRBNet number, and the dates, times, and individuals relevant to the situation. While individuals are encouraged to contact the Director or IO directly in order to facilitate their ability to thoroughly investigate issues, anonymous reports may be made utilizing the “Suggestions or Questions” submission link on the Academic Affairs home page on eWorkplace or the corporate compliance hotline (SilentWhistle).

14 Sponsored Research

It is BH policy that any sponsored research conducted under the auspices of the institution is conducted in accordance with federal guidelines and ethical standards.

The following describe the procedures required to ensure that all sponsored research meets this requirement.

14.1 Definitions

Sponsor Sponsor means the company, institution, individual donor, or organization responsible for the initiation, management or financing of a research study.

Sponsored research Sponsored research means research funded by external entities through a grant or contract that involves a specified statement of work (e.g., the research proposal) with a related transfer of value to the sponsor, including clinical trials involving investigational drugs, devices or biologics.

14.2 Responsibility

- 1) The Sponsored Programs Administration will review contracts and the IRB and Sponsored Programs Administration will share contract and study information as necessary for each sponsored protocol to ensure that protocol, consent, and contract language are consistent.
- 2) Contracts will be reviewed for the following by Sponsored Programs Administration as applicable to the individual project:
 - a) Sponsor contracts will indicate that the sponsor and Baystate will adhere to the protocol and applicable laws, regulations, and standards.
 - b) When appropriate, sponsor contracts will address responsibility for medical care for research-related injuries. It is the policy of Baystate that a clinical trial agreement must provide that when a subject sustains injury either from the drug or device or the requirements of the protocol, the sponsor must pay the costs associated with the treatment of the injury. An exception for the negligent or willful misconduct of Baystate or the investigator is acceptable.
 - c) If the sponsor will monitor the conduct of the research, the contract will contain provisions to ensure that findings that could affect the safety of subjects, subject's willingness to continue participation, or influence the conduct of the study or the IRB's approval, are promptly reported to Baystate.
 - d) When the sponsor is responsible for conducting data and safety monitoring, the

- e) Sponsor contracts will contain provisions regarding the dissemination of research results including the right of the Baystate investigator to publish results. The sponsor may retain the right to review prior to publication and in certain circumstances to delay publication for a reasonable time period.
- 3) Contracts will be compared with consent forms for consistency.

15 Participant Outreach

BH is committed to ensuring that educational opportunities are offered to research participants, prospective research participants, and community members in order to enhance their understanding of research involving human participants at BH.

The following procedures describe how BH fulfills that responsibility.

15.1 Responsibility

It is the responsibility of the HRPP Director or designee to implement the procedures outlined below.

15.2 Outreach Resources and Educational Materials

1. Baystate Health provides information about research on its external website. This includes resources for research participants including Frequently Asked Questions (FAQs), Research Contacts at Baystate Health, and relevant research-related links. The website also includes contact information for the HRPP Office so that research participants can communicate complaints, concerns, questions, or provide input on research participation.
2. The Academic Affairs home page on the internal website (eWorkplace) and the BH external website pages for research participants include a “Suggestions or Concerns” submission link.
3. The Research Participant’s Bill of Rights is provided in English and Spanish versions electronically on the BH external website, the HRPP/IRB internal website (eWorkplace), and in printed format for distribution and posting.
4. BH includes articles featuring research in its public magazine, Alphasights.
5. BH periodically provides presentations related to research to community organizations.

15.3 Evaluation

BH periodically evaluates its outreach activities and makes changes when appropriate. These evaluations take place in an informal, ongoing manner. All IRB staff, members and Chairs/ Vice Chairs will report both positive and negative feedback about all HRPP outreach activities to the HRPP Director. He/she will then track the input and any changes made to improve outreach activities. He/she will summarize that material annually. In order to formally evaluate its outreach activities, the HRPP Director will determine:

1. The specific community outreach activities being used
2. Whether or not these community outreach activities have an evaluative component,

3. The Website Content Analyst provides the HRPP Director with a quarterly report on number of times external website pages targeted to participants are access.
4. The external webpage “For Research Participants” contains a link to a survey soliciting feedback on the overall quality and usefulness of the website. The HRPP Director receives a notification upon completion of a survey and tracks results.
5. The HRPP Director will administer periodic surveys to determine the adequacy of outreach activities. The survey will assess:
 1. The scope, the content and the adequacy of outreach activities and resources.
 2. Whether the research community is using the HRPP website
 3. Whether the research community is using other educational materials to inform prospective participants about their rights and welfare as research participants.
 4. Whether additional resources are needed to improve participant outreach activities

The results of the survey will be used to establish both the adequacy of current outreach activities and any additional resources that may be needed to meet the needs of the research community regarding participant outreach.

16 Health Insurance Portability and Accountability Act (HIPAA)

The *Health Insurance Portability and Accountability Act of 1996* (HIPAA) required the creation of a Privacy Rule for identifiable health information. The resulting Privacy Rule, finalized in August 2002, set a compliance date of April 14, 2003. While the primary impact of the Privacy Rule is on the routine provision of and billing for health care, the Rule also affects the conduct and oversight of research.

The Privacy Rule defines individually identifiable health information transmitted or maintained by a covered entity in any form (electronic, written or oral) as “protected health information” (PHI) and establishes the conditions under which investigators may access and use this information in the conduct of research.

Except as otherwise permitted, the Privacy Rule requires that a research subject “authorize” the use or disclosure of his/her PHI to be utilized in the research. This authorization is distinct from the subject’s consent to participate in research, which is required under the Common Rule and FDA regulations.

Under the Privacy Rule, an Authorization may be combined with the consent document for research. When the consent document is combined with an Authorization as it is at Baystate, 45 CFR part 46 and/or 21 CFR parts 50 and 56 require IRB review of the combined document.

Additionally, the IRB, and for exempt projects and other categories of research not subject to IRB oversight, the HRPP, are designated at Baystate to act upon requests for waivers and alterations of the Authorization requirement for research purposes.

Protected Health Information may not be used internally or disclosed to any outside person or organization for research purposes at Baystate without prior approval of the IRB, or as described previously, the HRPP. BH researchers must also abide by all corporate [Patient Privacy](#) policies.

16.1 Definitions (per [HIPAA Privacy Booklet for Research](#))

Access Access is the mechanism of obtaining or using information electronically, on paper, or other medium for the purpose of performing an official function.

Accounting of Disclosures. Information that describes a covered entity’s disclosures of PHI other than for treatment, payment, and health care operations; disclosures made with Authorization; and certain other limited disclosures. For those categories of disclosures that need to be in the accounting, the accounting must include disclosures that have occurred during the 6 years (or a shorter time period at the request of the individual) prior to the date of the request for an accounting. However, PHI disclosures made before the compliance date for a covered entity are not part of the accounting requirement.

Authorization. An individual's written permission to allow a covered entity to use or disclose specified PHI for a particular purpose. Except as otherwise permitted by the Rule, a covered entity may not use or disclose PHI for research purposes without a valid Authorization.

Covered entity. A health plan, a health care clearinghouse, or a health care provider who transmits health information in electronic form in connection with a transaction for which HHS has adopted a standard.

Data Use Agreement. An agreement into which the covered entity enters with the intended recipient of a limited data set that establishes the ways in which the information in the limited data set may be used and how it will be protected.

Designated Record Set. A group of records maintained by or for a covered entity that includes (1) medical and billing records about individuals maintained by or for a covered health care provider; (2) enrollment, payment, claims adjudication, and case or medical management record systems maintained by or for a health plan; or (3) used, in whole or in part, by or for the covered entity to make decisions about individuals. A record is any item, collection, or grouping of information that includes PHI and is maintained, collected, used, or disseminated by or for a covered entity.

Disclosure. The release, transfer, access to, or divulging of information in any other manner outside the entity holding the information.

Health Information. Any information, whether oral or recorded in any form or medium, that (1) is created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university, or health care clearinghouse; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual.

Health Insurance Portability and Accountability Act of 1996 (HIPAA, The Privacy Rule). This Act requires, among other things, under the Administrative Simplification subtitle, the adoption of standards, including standards for protecting the privacy of individually identifiable health information.

Individually Identifiable Health Information. Information that is a subset of health information, including demographic information collected from an individual, and (1) is created or received by a health care provider, health plan, employer, or health care clearinghouse; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; and (a) that identifies the individual; or (b) with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

Limited Data Set. Refers to PHI that excludes 16 categories of direct identifiers and may be used or disclosed, for purposes of research, public health, or health care operations, without

obtaining either an individual's Authorization or a waiver or an alteration of Authorization for its use and disclosure, with a data use agreement.

Minimum Necessary. The least information reasonably necessary to accomplish the intended purpose of the use, disclosure, or request. Unless an exception applies, this standard applies to a covered entity when using or disclosing PHI or when requesting PHI from another covered entity. A covered entity that is using or disclosing PHI for research without Authorization must make reasonable efforts to limit PHI to the minimum necessary. A covered entity may rely, if reasonable under the circumstances, on documentation of IRB or Privacy Board approval or other appropriate representations and documentation under section 164.512(i) as establishing that the request for protected health information for the research meets the minimum necessary requirements.

Privacy Board. A board that is established to review and approve requests for waivers or alterations of Authorization in connection with a use or disclosure of PHI as an alternative to obtaining such waivers or alterations from an IRB. A Privacy Board consists of members with varying backgrounds and appropriate professional competencies as necessary to review the effect of the research protocol on an individual's privacy rights and related interests. The board must include at least one member who is not affiliated with the covered entity, is not affiliated with any entity conducting or sponsoring the research, and is not related to any person who is affiliated with any such entities. A Privacy Board cannot have any member participating in a review of any project in which the member has a conflict of interest.

Protected Health Information. PHI is individually identifiable health information transmitted by electronic media, maintained in electronic media, or transmitted or maintained in any other form or medium. PHI excludes education records covered by the Family Educational Rights and Privacy Act, as amended, 20 U.S.C. 1232g, records described at 20 U.S.C. 1232g(a)(4)(B)(iv), and employment records held by a covered entity in its role as employer.

Research. A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. This includes the development of research repositories and databases for research.

Use. With respect to individually identifiable health information, the sharing, employment, application, utilization, examination, or analysis of such information within the entity or health care component (for hybrid entities) that maintains such information.

Waiver or Alteration of Authorization. The documentation that the covered entity obtains from a researcher or an IRB or a Privacy Board that states that the IRB or Privacy Board has waived or altered the Privacy Rule's requirement that an individual must authorize a covered entity to use or disclose the individual's PHI for research purposes.

Workforce. Employees, volunteers, trainees, and other persons whose conduct, in the performance of work for a covered entity, is under the direct control of the covered entity, whether or not they are paid by the covered entity.

16.2 Authorization

Except as otherwise permitted, the Privacy Rule requires that a research subject “authorize” the use or disclosure of his/her PHI to be utilized in the research. This authorization is distinct from the subject’s consent to participate in research, which is required under the Common Rule and FDA regulations. Just as a valid consent under Common Rule and FDA regulations must meet certain requirements, a valid authorization must contain certain statements and core elements (45 CFR 164.508(c)). At Baystate, authorization language is to be incorporated into the consent document. Template consent documents, which include HIPAA authorization language, are available on the IRB eWorkplace web site.

Once executed, a signed copy must be provided to the individual providing authorization. Signed authorizations must be retained by the covered entity for 6 years from the date of creation or the date it was last in effect, whichever is later.

A research subject has the right to revoke their authorization at any time. Researchers are not required to retrieve information that was disclosed under the authorization before learning of the revocation. Additionally, researchers may continue to use and disclosure PHI already obtained for the research under an authorization to the extent necessary to protect the integrity of the research.

When an authorization is obtained for research purposes, the Privacy Rule requires that it pertain only to a specific research study, not to nonspecific research or to future, unspecified projects. The Privacy Rule considers the creation and maintenance of a research repository or database as one specific research activity, the subsequent use or disclosure by a covered entity of information from the database for a specific research study will require separate authorization unless a waiver of the requirement is granted.

When an Authorization permits disclosure of PHI to a person or organization that is not a covered entity (such as a sponsor or funding source of the research), the Privacy Rule does not continue to protect the PHI disclosed to such entity. However, other Federal and State laws may establish continuing protections for the disclosed information. Under the HHS Protection of Human Subjects Regulations or the FDA Protection of Human Subjects Regulations, an IRB may impose further restrictions on the use or disclosure of research information to protect subjects.

Authorization Core Elements:

1. A description of the PHI to be used or disclosed, identifying the information in a specific and meaningful manner.
2. The names or other specific identification of the person or persons (or class of persons) authorized to make the requested use or disclosure.
3. The names or other specific identification of the person or persons (or class of persons) to whom the covered entity may make the requested use or disclosure.

4. A description of each purpose of the requested use or disclosure.
5. Authorization expiration date or expiration event that relates to the individual or to the purpose of the use or disclosure (“end of the research study” or “none” are permissible for research, including for the creation and maintenance of a research database or repository).
6. Signature of the individual and date. If the individual’s legally authorized representative signs the Authorization, a description of the representative’s authority to act for the individual must also be provided.

Authorization Required Statements:

1. A statement of the individual’s right to revoke his/her Authorization and how to do so, and, if applicable, the exceptions to the right to revoke his/her Authorization or reference to the corresponding section of the covered entity’s notice of privacy practices.
2. Whether treatment, payment, enrollment, or eligibility of benefits can be conditioned on Authorization, including research-related treatment and consequences of refusing to sign the Authorization, if applicable.
3. A statement of the potential risk that PHI will be re-disclosed by the recipient. This may be a general statement that the Privacy Rule may no longer protect health information disclosed to the recipient.

16.3 Waiver or Alteration of the Authorization Requirement

Obtaining signed authorization to access and use of PHI for research is not always feasible. The Privacy Rule contains criteria for waiver or alterations of authorization. If a covered entity has used or disclosed PHI for research pursuant to a waiver or alteration of authorization, documentation of the approval of the waiver or authorization must be retained for 6 years from the date of its creation or the date it was last in effect, whichever is later.

For research uses and disclosures of PHI, an IRB or Privacy Board may approve a waiver or an alteration of the authorization requirement in whole or in part. A complete waiver occurs when the IRB or Privacy Board determines that no authorization will be required for a covered entity to use and disclose PHI for a particular research project. A partial waiver of authorization occurs when an IRB or Privacy Board determines that a covered entity does not need authorization for all PHI uses and disclosures for research purposes, such as accessing PHI for research recruitment purposes. An IRB or Privacy Board may also approve a request that removes some PHI, but not all, or alters the requirements for an authorization (an alteration).

In order for the IRB to waive or alter authorization, the Privacy Rule (45 CFR 164.512(i)(2)(ii)) requires the IRB to determine the following:

1. The use or disclosure of the PHI involves no more than minimal risk to the privacy of individuals based on, at least, the presence of the following elements:
 - a. An adequate plan to protect health information identifiers from improper use and disclosure.
 - b. An adequate plan to destroy identifiers at the earliest opportunity consistent with conduct of the research (absent a health or research justification for retaining them or a legal requirement to do so).
 - c. Adequate written assurances that the PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.
2. The research could not practicably be conducted without the waiver or alteration.
3. The research could not practicably be conducted without access to and use of the PHI.

The Privacy Rule allows a waiver or an alteration of Authorization obtained from a single IRB or Privacy Board to be used to obtain PHI in connection with a multi-site project. However, HHS also recognizes that “covered entities may elect to require duplicate IRB or Privacy Board reviews before disclosing [PHI] to requesting researchers” (67 *Federal Register* 53232, August 14, 2002). At Baystate, PHI may not be disclosed for the purposes of research pursuant to a waiver provided by a non-BH IRB or Privacy Board without the approval of the HRPP or IRB.

16.4 Activities Preparatory to Research

Under the preparatory to research provision of the Privacy Rule, a covered entity may permit a researcher who works for that covered entity to use PHI for purposes preparatory to research such as assessing the feasibility of conducting a research project, developing a grant application, or identifying potential subjects. A covered entity may also permit, as a disclosure of PHI, a researcher who is not a workforce member of that covered entity to review PHI (within that covered entity) for purposes preparatory to research.

The covered entity must obtain from a researcher representations that (1) the use or disclosure is requested solely to review PHI as necessary to prepare a research protocol or for similar purposes preparatory to research, (2) the PHI will not be removed from the covered entity in the course of review, and (3) the PHI for which use or access is requested is necessary for the research.

At BH, this is accomplished by the investigator submitting either a Preparatory to Research form (for projects in development) or a request for waiver of consent and authorization for screening purposes via IRBNet.

16.5 Future Uses: Databases and Repositories

The Privacy Rule recognizes the creation of a research database or a specimen repository to be a research activity if the data/specimens to be stored contain PHI. There are two separate activities that the covered entity must consider: (1) The use or disclosure of PHI for creating a research database or repository and (2) The subsequent use or disclosure of PHI in the database for a particular research protocol. Further, when an Authorization is obtained for research purposes, the Privacy Rule requires that it pertain only to a specific research study, not to nonspecific research or to future, unspecified projects. Thus the authorization to include PHI in a database and/or specimen repository must specify the research purpose for which the use or disclosure will occur (the storage in the research database or specimen repository).

Subsequently, when that PHI is to be accessed for a specific research project, authorization for use or disclosure for the specific research project must be obtained unless a waiver of the requirement is sought and approved. De-identification of the data or release as a limited data set with a data use agreement are alternative considerations that may be useful in certain circumstances.

Research-related treatment cannot be conditioned on participation in future unspecified research, such as the collection and storage of data/samples for future vague research. For example, a covered entity that conducts an interventional clinical trial that also involves collecting tissues and associated PHI for storage in a central repository for future research would not be permitted to obtain a compound authorization for both research purposes if research-related treatment is conditioned upon signing the authorization for the clinical trial. Separate, distinct authorizations are required; one for the clinical trial and one for the research repository. At BH, since authorization language is incorporated into the consent document, two consent/authorization documents will be required; one for the clinical trial itself and one for the repository or “bank”.

16.6 De-identification of PHI under the Privacy Rule

Covered entities may use or disclose health information that is de-identified without restriction under the Privacy Rule. The “Safe Harbor” method permits a covered entity to de-identify data by removing all 18 elements that could be used to identify the individual or the individual’s relatives, employers, or household members. The covered entity also must have no actual knowledge that the remaining information could be used alone or in combination with other information to identify individuals. Under this method, the identifiers that must be removed are the following:

- 1) Names.
- 2) All geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP Code, and their equivalent geographical codes, except for the initial three digits of a ZIP Code if, according to the current publicly available data from the Bureau of the Census:

- a. The geographic unit formed by combining all ZIP Codes with the same three initial digits contains more than 20,000 people.
 - b. The initial three digits of a ZIP Code for all such geographic units containing 20,000 or fewer people are changed to 000.
- 3) All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.
- 4) Telephone numbers.
- 5) Facsimile numbers.
- 6) Electronic mail addresses.
- 7) Social security numbers.
- 8) Medical record numbers.
- 9) Health plan beneficiary numbers.
- 10) Account numbers.
- 11) Certificate/license numbers.
- 12) Vehicle identifiers and serial numbers, including license plate numbers.
- 13) Device identifiers and serial numbers.
- 14) Web universal resource locators (URLs).
- 15) Internet protocol (IP) address numbers.
- 16) Biometric identifiers, including fingerprints and voiceprints.
- 17) Full-face photographic images and any comparable images.
- 18) Any other unique identifying number, characteristic, or code, unless otherwise permitted by the Privacy Rule for re-identification.

Alternatively, a qualified statistician may certify that the risk is very small that health information could be used, alone or in combination with other available information, to identify individuals. The qualified statistician must document the methods and results of the analysis that justify such a determination. This analysis must be retained by the covered entity for 6 years from the date of its creation or when it was last acted on, whichever is later.

The Privacy Rule permits a covered entity to assign to, and retain with, the de-identified health information, a code or other means of record re-identification if that code is not derived from or related to the information about the individual and is not otherwise capable of being translated to identify the individual. The covered entity may not use or disclose the code or other means of record identification for any other purpose and may not disclose its method of re-identifying the information.

NOTE: Data that is considered de-identified under HIPAA may still be considered human subjects data under the Common Rule, particularly when working with a small data set that can be further broken down into smaller subsets. Additionally, while coded information may be de-identified under HIPAA, if the researcher holds or has the ability to access both the code and the data, the information is considered identifiable private information under the Common Rule.

16.7 Limited Data Sets and Data Use Agreements

Limited data sets are data sets stripped of certain direct identifiers. Limited data sets may be used or disclosed only for public health, research, or health care operations purposes. Because limited data sets may contain identifiable information, they are still PHI and as such are not considered de-identified under the Privacy Rule. Unlike de-identified data, protected health information in limited data sets may include: addresses other than street name or street address or post office boxes, all elements of dates (such as admission and discharge dates) and unique codes or identifiers not listed as direct identifiers. The following direct identifiers must be removed for PHI to qualify as a limited data set: (1) Names; (2) postal address information, other than town or city, state, and ZIP code; (3) telephone numbers; (4) fax numbers; (5) email addresses; (6) social security numbers; (7) medical record numbers; (8) health plan beneficiary numbers; (9) account numbers; (10) certificate or license numbers; (11) vehicle identifiers and license plate numbers; (12) device identifiers and serial numbers; (13) URLs; (14) IP addresses; (15) biometric identifiers; and (16) full-face photographs and any comparable images.

Before disclosing a limited data set a covered entity must enter into a data use agreement with the recipient, even when the recipient is a member of its workforce. The data use agreement establishes the parameters around the proposed uses and disclosures of the data, who is permitted to have access to the data, and stipulates that no other use will be made of the data, no attempt will be made to identify or contact individuals whose data are included in the limited data set, and that appropriate safeguards are in place to protect the data from unauthorized use. Data Use Agreements for the purposes of research are available through the HRPP/IRB office. Data Use Agreements should be uploaded into IRBNet along with the other project materials so that Baystate has a record of the agreement.

16.8 Research Subject Access to PHI

With few exceptions, the Privacy Rule guarantees individuals access to their medical records and other types of health information. One exception is during a clinical trial, when the subject's right of access can be suspended while the research is in progress. The subject must have been notified of and agreed to the temporary denial of access when providing consent and authorization. Any such notice must also inform the individual that the right to access will be restored upon conclusion of the clinical trial. Language accommodating this exclusion is included in the applicable BH research consent/authorization templates.

16.9 Accounting of Disclosures

The Privacy Rule generally grants individuals the right to a written “Accounting of Disclosures” of their Protected Health Information made by a covered entity without the individual’s authorization in the six years prior to their request for an Accounting. A covered entity must therefore keep records of such PHI disclosures for 6 years.

It is important to understand the difference between a use and a disclosure of PHI. In general, the use of PHI means communicating that information within the covered entity. A disclosure of PHI means communicating that information to a person or entity outside the covered entity. The Privacy Rule restricts both uses and disclosures of PHI, but it requires an accounting only for certain PHI disclosures.

Generally, an Accounting of Disclosures is required for:

- 1) Routinely Permitted Disclosures (e.g., under public health authority, to regulatory agencies, to persons with FDA-related responsibilities) with limited exceptions (e.g., law enforcement, national security, etc.)
- 2) Disclosures made pursuant to:
 - a. Waiver of Authorization
 - b. Research on Decedents’ Information
 - c. Reviews Preparatory to Research

An accounting is not needed when the PHI disclosure is made:

- 1) For treatment, payment, or health care operations.
- 2) Under an Authorization for the disclosure.
- 3) To an individual about himself or herself.
- 4) As part of a limited data set under a data use agreement.

The Privacy Rule allows three methods for accounting for research-related disclosures that are made without the individual's Authorization or other than a limited data set: (1) A standard approach, (2) a multiple-disclosures approach, and (3) an alternative for disclosures involving 50 or more individuals. Whatever approach is selected, the accounting is made in writing and provided to the requesting individual. Accounting reports to individuals may include results from more than one accounting method.

See Baystate Policy [BC 7.110](#) for a detailed discussion on Accounting for Disclosures.

16.10 Information Security

Baystate Health has established standards and safeguards to protect patient’s information and to ensure compliance with federal and state information security regulations. It is the

responsibility of investigators to familiarize themselves with and comply with these standards. The use of personal laptops, desktops, USB drives, and other non-Baystate devices for storage of research data is discouraged. In the instances when a non-Baystate computer or device must be utilized for the purposes of storing, even temporarily, or transmitting PHI or PII (Personally Identifiable Information) for research, the safeguards of the device must be verified by Information Services and a User Agreement completed. Additionally, any potential or known breach of a device or of research data must be immediately reported to both the IRB and Corporate Compliance so that appropriate steps can be taken to assess the situation, protect the information, and comply with regulations. Lost or stolen BH devices must also be reported to BMC Security.

Provisions for Data Security must be described in applications to the IRB and updated as necessary. When information containing direct identifiers such as Social Security Numbers or PHI including data considered sensitive is to be transferred outside of the institution, the provisions for data security may be subject to further review and approval by the Information Security Officer.

See the Baystate [Policies on Patient Privacy and Security](#) for further information.

17 Special Topics

17.1 Certificate of Confidentiality (CoC)

Certificates of Confidentiality are issued by the National Institutes of Health (NIH) to protect identifiable research information from forced disclosure. They allow the investigator and others who have access to research records to refuse to disclose identifying information on research participants in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. A CoC does not protect against voluntary disclosures by the researcher, but those disclosures must be specified in the informed consent form. A researcher may not rely on the Certificate to withhold data if the participant consents in writing to the disclosure.

Generally, any research project that collects personally identifiable, sensitive information and that has been approved by an IRB operating under either an approved Federal-Wide Assurance issued by the Office of Human Research Protections or the approval of the Food and Drug Administration is eligible for a Certificate. Federal funding is not a prerequisite for an NIH-issued Certificate, but the subject matter of the study must fall within a mission area of the National Institutes of Health, including its Institutes, Centers and the National Library of Medicine.

17.1.1 Statutory Basis for Protection

Protection against compelled disclosure of identifying information about subjects of biomedical, behavioral, clinical, and other research is provided by the Public Health Service Act §301(d), 42 U.S.C. §241(d):

"The Secretary may authorize persons engaged in biomedical, behavioral, clinical, or other research (including research on mental health, including research on the use and effect of alcohol and other psychoactive drugs) to protect the privacy of individuals who are the subject of such research by withholding from all persons not connected with the conduct of such research the names or other identifying characteristics of such individuals. Persons so authorized to protect the privacy of such individuals may not be compelled in any Federal, State or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals."

17.1.2 Usage

Certificates of Confidentiality may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation. By protecting researchers and institutions from being compelled to disclose information that would identify research subjects, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by assuring confidentiality and privacy to subjects.

Any investigator engaged in research in which sensitive information is gathered from human subjects (or any person who intends to engage in such research) may apply for a Certificate of Confidentiality. Research can be considered "sensitive" if it includes:

1. Research on HIV, AIDS, and STDs;
2. Information about sexual attitudes, preferences, practices;
3. Information about personal use of alcohol, drugs, or other addictive products;
4. Information about illegal conduct;
5. Information that could damage an individual's financial standing, employability, or reputation within the community;
6. Information in a subject's medical record that could lead to social stigmatization or discrimination; or
7. Information about a subject's psychological well-being or mental health.
8. Genetic studies, including those that collect and store biological samples for future use;
9. Research on behavioral interventions and epidemiologic studies.

This list is not exhaustive. Researchers contemplating research on a topic that might qualify as sensitive should contact the HRPP office for further information.

In the consent form, investigators should tell research subjects that a Certificate is in effect. Subjects should be given a fair and clear explanation of the protection that it affords, including the limitations and exceptions. Every research project that includes human research subjects should explain how identifiable information will be used or disclosed, regardless of whether or not a Certificate is in effect.

17.1.3 Limitations

The protection offered by a Certificate of Confidentiality is not absolute. A Certificate protects research subjects only from legally compelled disclosure of their identity. It does **not** restrict voluntary disclosures.

For example, a Certificate does not prevent researchers from voluntarily disclosing to appropriate authorities such matters as child abuse, a subject's threatened violence to self or others, or from reporting a communicable disease. However, if researchers intend to make such disclosures, this should be clearly stated in the informed consent form which research subjects are asked to sign.

In addition, a Certificate of Confidentiality does **not** authorize the person to whom it is issued to refuse to reveal the name or other identifying characteristics of a research subject if

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

17.1.4 Application Procedures

Any person engaged in research collecting sensitive information from human research subjects may apply for a Certificate of Confidentiality. For most research, Certificates are obtained from NIH. If NIH funds the research project, the investigator may apply through the funding Institute. However, even if the research is not supported with NIH funding, the investigator may apply for a Certificate through the NIH Institute or Center (IC) funding research in a scientific area similar to the project.

If the research is conducting a sensitive research project that is covered by the AHRQ confidentiality statute (42 U.S.C. section 299a-1(c) entitled “limitation on use of certain information”) or the Department of Justice confidentiality statute (42 USC section 3789g), then a CoC is not required.

If there is an Investigational New Drug Application (IND) or an Investigational Drug Exemption (IDE), the sponsor can request a CoC from the FDA.

For more information, see the [NIH Certificates of Confidentiality Kiosk](#).

17.2 Mandatory Reporting

While any person may make a report if they have reasonable cause to believe that a child, disabled person or elder was abused or neglected, Massachusetts law mandates that certain persons who suspect abuse or neglect of a child, elder or disabled person report this to the appropriate agencies.

In situations where conditions of abuse or neglect might be revealed, mandated reporters should make themselves known as such via the consent process to parents of children under age 18, to subjects who are children, and to subjects who are potential victims of abuse or neglect.

BH [Clinical Operations Policies](#) describe the requirements of Massachusetts law for reporting abuse or neglect to the appropriate state agency:

CO 9.610 Child Abuse and Neglect (M.G.L.c. 119, sec. 51A et seq), the Department of Child and Family Services

CO 9.620 Reporting Elder Abuse (M.G.L.c. 19A, §15), the Department of Elder Affairs

CO 9.625 Reporting Abuse of Disabled Persons (M.G.L.c. 19C, sections 1-10), the Disabled Persons Protection Commission

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

17.3 Student Research

17.3.1 Human Subjects Research and Course Projects

Learning how to conduct ethical human subjects research is an important part of a student's educational experience. Research activities that are designed as part of a course requirement for purposes of learning experience only and are **NOT *designed to develop or contribute to generalizable knowledge*** **MAY not** require IRB review and approval if all of the following conditions are true:

- Results of the research are viewed only by the course instructor for teaching purposes and discussed within the classroom for teaching and learning purposes.
- Results of the research are not made public through presentation (outside of the classroom) and are not published in paper or electronic format (e.g., cannot be made available on the internet, cannot be published in a journal, etc.).
- Research procedures are no more than minimal risk.
- Vulnerable populations are not targeted (e.g., children under age 18, prisoners, persons who are cognitively impaired, etc.).
- Data collected are recorded in such a manner that the subjects are not identifiable (Images in videotapes and photographs and voices on audiotape are identifiable.)
- When appropriate, an informed consent process is in place.

Responsibility of the Course Instructor: The course instructor is responsible for communicating to the students the ethics of human subjects research, for ensuring the protection of human subjects (including a process is in place for obtaining voluntary informed consent from research subjects when appropriate), and for monitoring the students' progress.

When designing a project, students should be instructed on the ethical conduct of research and on the preparation of the IRB application when such is required. In particular, instructors and students should:

- understand the elements of informed consent;

- develop appropriate consent documents;
- plan appropriate strategies for recruiting subjects;
- identify and minimize potential risks to subjects;
- assess the risk-benefit ratio for the project;
- establish and maintain strict guidelines for protecting confidentiality, and
- allow sufficient time for IRB review (if necessary) and completion of the project.

In making a determination of whether or not a class research project requires IRB review, the instructor is encouraged to err on the side of caution and to contact the IRB office for assistance.

Individual Research Projects Conducted by Students

Independent study projects, senior theses, undergraduate research projects, masters and advanced degree research, and similar exercises may very well be intended to develop or contribute to generalizable knowledge and thus are subject to IRB review. It is important to keep in mind that any human subjects research activity must go through the IRB review process prior to enrolling subjects and collecting data. **IRB review cannot occur after a study has begun.**

Students and advisors should contact the HRPP/IRB Office with any questions.

17.4 Genetic Studies

Genetic research studies may create special risks to human subjects and their relatives. These involve medical, psychosocial, and economic risks, such as the possible loss of privacy, insurability, and employability, change in immigration status and limits on education options, and may create a social stigma. Knowledge of one's genetic make-up may also affect one's knowledge of the disease risk status of family members.

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

1. Will test results be given?
2. Will disease risk be quantified, including the limits on certainty of the testing?
3. Will a change in a family relationship be disclosed, such as mistaken paternity?
4. Does the subject or family member have the option not to know the results? How will this decision be recorded?
5. Could other clinically relevant information be uncovered by the study? How will disclosure of this added information occur?

6. Do any practical limitations exist on the subject's right to withdraw from the research, withdraw data, and/or withdraw DNA?
7. Is the subject permitted to participate in the study while refusing to have genetic testing (such as in a treatment study with a genetic testing component)?

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

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

Special Considerations under Federal, State and Municipal Law

Federal law: The Genetic Information Nondiscrimination Act (GINA) prohibits health insurance companies and group health plans from using genetic information for coverage decisions and employers with 15 or more employees from using genetic information to make employment decisions. GINA became effective for health insurers and plans during 2009 and will become effective for employers in 2010. Once effective, GINA protects all genetic information, even if the testing occurred before the effective dates.

“Genetic information” means information any request for or receipt of genetic services or participation in clinical research that includes genetic testing, counseling or education by the subject or the subject’s family members.

“Genetic testing” means an analysis of human DNA, RNA, chromosomes, proteins or metabolites that detect genotypes, mutations, or chromosomal changes.

The OHRP has issued guidance on GINA and its implications for investigators and IRBs.

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

Also, Massachusetts laws provide nondiscrimination provisions similar to GINA, not only for health insurers and health plans, but also for life, disability and long-term care insurers.

Ordinances of the City of Springfield: The Biomedical Research Regulations of the City of Springfield addresses the use of recombinant DNA (rDNA). It requires that any use of rDNA within the City must be done in conformity with federal law and regulations, including mandatory review by an Institutional Biosafety Committee. Title 5, Chapter 5.42.

Consent: In order to comply with Massachusetts law and provide adequate information to subjects about GINA’s protections, the BH consent template contains required text to be included for any protocol that involves genetic information.

17.5 Research Involving Coded Private Information or Biological Specimens

BH policy is based on the OHRP guidance document entitled, “**Guidance on Research Involving Coded Private Information or Biological Specimens**” (October 16, 2008 <http://www.hhs.gov/ohrp/policy/cdebiol.html>). This document:

1. Provides guidance as to when research involving coded private information or specimens is or is not research involving human subjects, as defined under HHS regulations for the protection of human research subjects (45 CFR part 46).
2. Reaffirms OHRP policy that, under certain limited conditions, research involving **only** coded private information or specimens is not human subjects research.
3. Clarifies the distinction between (a) research involving coded private information or specimens that does not involve human subjects and (b) human subjects research that is exempt from the requirements of the HHS regulations.
4. References pertinent requirements of the HIPAA Privacy Rule that may be applicable to research involving coded private information or specimens.

Note: The FDA definition of human subjects differs from the Common Rule definition. Use of coded specimens for FDA-regulated research such as research on In Vitro Diagnostic Devices requires assessment according to the FDA regulations and guidelines. Investigators should contact the HRPP/IRB office for guidance.

For purposes of this policy, *coded* means that: (1) identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and (2) a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

Guidance:

Obtaining identifiable private information or identifiable specimens for research purposes constitutes human subjects research. *Obtaining* identifiable private information or identifiable specimens includes, but is not limited to:

1. Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens that have been provided to the investigator from any source; and

2. Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens that were already in the possession of the investigator.

In general, private information or specimens are considered to be individually identifiable when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

Private information or specimens are not considered to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

Research involving **only** coded private information or specimens do **not** involve human subjects per the Common Rule definition if both of the following conditions are met:

1. The private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and
2. The investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
 1. The investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement);
 2. There are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
 3. There are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

In some cases an investigator who obtains coded private information or specimens about living individuals under one of the conditions cited in 2(a)-(c) above may (1) unexpectedly learn the identity of one or more living individuals, or (2) for previously unforeseen reasons now believe that it is important to identify the individual(s). If, as a result, the investigator knows, or may be able to readily ascertain, the identity of the individuals to whom the previously obtained private information or specimens pertain, then the research activity now would involve human subjects. Unless this human subjects research is determined to be exempt (See Section 3.3), IRB review of the research would be required. Informed consent of the subjects also would be required unless the IRB approved a waiver of informed consent (See Section 5.9).

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

The responsibility for initial determination as to whether an activity constitutes human subjects research rests with the investigator. The investigator should make this determination based on the definitions of “human subject” and “research” in Section 1.3. Since the institution will hold them responsible if the determination is not correct, investigators are urged to prospectively request a confirmation that an activity does not constitute human subjects research from the Human Research Protection Program. The request should be made by the submission of an on-line request for a Human Subjects Research Determination via IRBNet. See Section 3.2.

17.6 Case Reports Requiring IRB Review

In general, an anecdotal retrospective report on a single patient or small series (up to 3) of patients seen in one’s own practice and a comparison of these patients to existing reports in the literature is not research and would not require IRB approval. Going beyond one’s own practice to seek out and report cases seen by other clinicians creates the appearance of a systematic investigation with the intent to contribute to generalizable knowledge and therefore would be considered research and would require IRB approval.

All BH policies on the protection of patient(s) privacy and confidentiality (including the HIPAA compliance policies) and the principles of the Belmont Report apply. Clinicians should be especially sensitive to protecting the privacy of individuals with unique or unusual diagnoses or illnesses that could result in the individual being identified or recognized.

17.6.1 Definitions

Single Case Report: The external reporting (e.g., publication or poster/verbal presentation) of an interesting clinical situation or medical condition of a single patient. Case reports normally contain detailed information about an individual patient and may include demographic information and information on diagnosis, treatment, response to treatment, follow-up after treatment, as well as a discussion of existing relevant literature. The patient information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience.

Case Series: The external reporting (e.g., publication or poster/verbal presentation) of an interesting clinical situation or medical condition in a series of patients (i.e., more than one patient). Case series usually contain detailed information about each patient and may include demographic information and information on diagnosis, treatment, response to treatment, follow-up after treatment, as well as a discussion of existing relevant literature. The information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience.

17.7 Teaching Activities

Presentation of clinical information in the context of medical education, such as at teaching conferences, does not require IRB review. Instructional information presented by healthcare providers in traditional educational settings that include discussion of the clinical care of one or more patients, such as commonly occurs in a conference on clinical management, is not considered research requiring IRB review if the scope of the comments are limited to the specific educational setting. A useful guide to distinguish this type of activity from research is if the speaker prefaces the comments by, "In my experience, ..." or implies this in the manner of presentation. Such a presentation by Baystate Medical Center faculty may occur outside of Baystate Medical Center including continuing medical education, presentations at professional meetings, and even in published form as opinions in medical journals as long as the statements are clearly identified as representing the personal experience and knowledge of the presenter and not the result of separate, formal clinical research.

17.8 Community Based Participatory Research (CBPR)

Community based research is research that is conducted as an equal partnership between academic investigators and members of a community. In CBPR projects, the community participates fully in all aspects of the research process. *Community* is often self-defined, but general categories of community include geographic community, community of individuals with a common problem or issue, or a community of individuals with a common interest or goal.

Where research is being conducted in communities, PIs are encouraged to involve members of the community in the research process, including the design and implementation of research and the dissemination of results when appropriate. The HRPP Office will assist the PI in developing such arrangements.

The following are some questions that PIs should ask as they develop CBR. These are also the questions that the IRB should consider when reviewing CBR.

17.8.1 CBR Questions

Background, purpose, objectives

How was the community involved or consulted in defining the need?

Who came up with the research objectives and how?

Is this research really justified with respect to community concerns?

Are there concrete action outcomes?

Who benefits? How?

Research methodology

How will the community be involved in the research? At what levels?

What training or capacity-building opportunities will be built in?

Procedures

Will the methods used be sensitive and appropriate to various communities (consider literacy issues, language barriers, cultural sensitivities, etc.)?

How will scientific rigor and accessibility be balanced?

Participants

Are the appropriate people being included to get the questions answered (e.g., service providers, community members, leaders etc.)?

How will the research team protect vulnerable groups?

Will the research process include or engage marginalized or disenfranchised community members? How?

Is there a reason to exclude some people? Why?

Recruitment

What provisions have been put in place to ensure culturally-relevant and appropriate recruitment strategies and materials?

Have “power” relationships been considered in the recruitment strategies to minimize coercion?

Who approaches people about the study and how?

Risks and benefits

What are the risks and benefits of the research for communities? For individuals?

Are the risks (including risks to the community) being presented honestly?

How will risks be minimized?

Privacy and confidentiality

Where will data be stored? Who will have access to the data? How?

What processes will be put in place to be inclusive about data analysis and yet maintain privacy of participants?

What will be the rules for working with transcripts or surveys with identifying information?

How will boundaries between multiple roles (e.g., researcher, counselor, peer) be maintained?

Compensation

How will people be reimbursed for their time and honor their efforts without it becoming coercive.

How will compensation be approached?

What provisions have been made for minimizing barriers to participation (e.g., providing for food, travel, childcare)?

Who is managing the budget? How are these decisions negotiated?

Conflicts of interest

What happens when the PI/research staff is the friend, peer, service provider, doctor, nurse, social worker, educator, funder, etc.

How will power differentials be appropriately acknowledged and negotiated?

Informed consent process

What does informed consent mean for “vulnerable” populations (e.g., children, mentally ill, developmentally challenged)?

What processes are in place for gathering individual consent?

Where written informed consent is not being obtained, explain why.

What processes are in place for gathering community consent?

Where minors are to be included as participants, how will assent be obtained?

Are the consent processes culturally sensitive and appropriate for the populations being included?

Outcomes and results

How will the research be disseminated to academic audiences?

How will the research be disseminated to community audiences?

What are the new ways that this research will be acted upon to ensure community/policy/social change?

Ongoing reflection and partnership development

Is there a partnership agreement or memorandum of understanding to be signed by all partners that describes how they will work together?

What internal process evaluation mechanisms are in place?

When plans change to accommodate community concerns (as they invariably do in CBR), how will this be communicate to the IRB?

Based on:

Ethical Dilemmas in Community-Based Participatory Research: Recommendations for Institutional Review Boards

Sarah Flicker, Robb Travers, Adrian Guta, Sean McDonald, and Aileen Meagher

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17.9 Quality Improvement & Quality Assurance Activities

The HRPP and IRBs are frequently presented with questions regarding when Quality Improvement (QI) activities also meet the definition of human subjects research requiring IRB review and approval. It is essential to understand that projects may be both QI and human subjects research. The following materials are included to assist the investigator and the IRB in assessing whether or not individual projects require IRB review and approval.

Quality Improvement has been described as follows by the National Bioethics Advisory Commission in its August 2001 document titled “Ethical and Policy Issues in Research Involving Human Participants” (page 37):

“These activities, generally referred to as program evaluation or quality improvement, are not intended to have any application beyond the specific organization in which they are conducted. As is true in the area of public health, because populations are the subject of study and because the methods used in program evaluation or quality improvement are the same as those used in research, it is often difficult to determine whether an activity is research that falls under the oversight system.

Definitional issues regarding program evaluation or quality improvement are not limited to health care delivery. They also occur in industrial or educational settings and in social science and operations research. However, if the purpose is to assess the success of an established program, and the information gained from the evaluation will be used to improve that program, the activity should not be considered research involving human participants. Evaluation is a program monitoring tool, and the information gained will immediately benefit the program and/or the individuals involved.

However, when quality improvement involving human participants is undertaken to test a new, modified, or previously untested intervention, service, or program to determine whether it is effective and can be used elsewhere, the activity is human participant research and subject to the oversight system.”

Definitions:

Research: (See Section 1 for a detailed definition)

Common Rule: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge.

FDA: An experiment involving a FDA-regulated test article and one or more human subjects.

Quality improvement: a systematic pattern of actions that is constantly optimizing productivity, communication and value within an organization in order to achieve the aim of measuring the attributes, properties, and characteristics of a product/service in the context of the expectations and needs of customers and user of that product. (Institute of Medicine)

Comparison:

	Research	Quality Improvement
Goal	Advance general knowledge in academic, scientific or professional community: generate, evaluate or confirm explanatory theory or conclusion and invite critical appraisal by peers through presentation/debate in public forums	Improve patient care, a clinical program or service: identify specific services, protocols, clinical practices, or clinical processes/outcomes within a department, clinical program or facility for improvement
Literature review	Organized review of relevant literature	Available literature and comparative data, or clinical programs, practices or protocol at other institutions to design improvement plan; do not plan full scientific literature reviews
Research design	Leads to scientifically valid findings (control groups, random subject selection, statistical tests)	Established quality improvement methods (e.g. PDSA cycle) aimed at producing change. Does not include sufficient research design elements to support scientifically valid findings
Benefit	Subjects may not derive personal benefit from the knowledge gained	Most patients who participate <i>are expected to benefit</i> from the knowledge gained
Risk	May impose risk or burden on patients	Does not impose any risk or burden on patients

**Provided by the Center for Quality of Care Research (Modified from Cambridge Health Alliance)*