

Brown University

Human Research Protection Program

Policy and Procedure Manual

Approved: December, 2011

Revised: June 5, 2018; January 29, 2019, April 5, 2019, May 4, 2020, July 24, 2020, August 20, 2020, March 1, 2022, October 7, 2022

# Human Research Protection Program (HRPP)

## Mission:

Brown University fosters a research environment that promotes the respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of the University. In the review and conduct of research, actions by the University will be guided by the principles set forth in the [Belmont Report](http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm). The actions of the University will also conform to all applicable federal, state, and local laws and regulations.

In order to fulfill this mission, the University has established a Human Research Protection Program (HRPP). The mission of the HRPP is to:

* + - safeguard and promote the health and welfare of human research participants by ensuring that their rights, safety, and well-being are protected;
		- provide timely and high quality education, review and monitoring of human research projects; and
		- facilitate excellence in human research. The HRPP includes mechanisms to:
		- Establish a formal process to monitor and evaluate and continually improve the protection of human participants in research
		- Dedicate resources sufficient to do so
		- Educate investigators and research staff about their ethical responsibility to protect research participants
		- When appropriate, intervene in research and respond directly to concerns of research participants

## Institutional Authority

The operating procedures in this HRPP Manual serve as the governing procedures for the conduct and review of all human research conducted under the auspices of Brown University. The HRPP Manual is made available to all Brown University investigators and research staff and is posted on the Office of Research Integrity (ORI) website.

## Ethical Principles

Brown University is committed to conducting research with the highest regard for the welfare of human participants. It upholds, and adheres to, the principles of *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* by the National Commission for the Protection of Human Subjects in 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 assured by ensuring that possible benefits are maximized and possible risks are minimized to all participants.
3. Justice, the equitable selection of participants.

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

## Regulatory Compliance

The HRPP is responsible for ensuring compliance with federal regulations, state law, and institutional policies. All human research at Brown University is conducted in accordance with the policy and regulations found in 45 CFR 46 and 21 CFR 50 and 56. The actions of Brown University will also conform to all other applicable federal, state, and local laws and regulations.

## Federalwide Assurance (FWA) and IRB (IORG) number

The HRPP operates under the authority of its current Federalwide Assurance (FWA00004460) and provides support to an independent Institutional Review Board (IRB), which reviews all human research protocols that meet the federal definition of human subjects research. Brown University’s IRB Organization (IORG) number for its registration with OHRP is: IORG0000315.

## Institutional Official

The ultimate responsibility of the HRPP resides with the Vice President for Research (VPR), who serves as the Institutional Official (IO) of the program. The IO is responsible for ensuring the Brown University HRPP has the resources and support necessary to comply with all institutional policies and with federal regulations and guidelines that govern human research. The IO is legally authorized to represent Brown University. He/she is the signatory of the FWA and assumes the obligations of the FWA. The IO is the point of contact for correspondence addressing human research

with the DHHS Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA), and any other federal regulatory agencies.

The IO also holds ultimate responsibility for oversight of the Institutional Review Board (IRB) and all Brown University investigators; for assuring the IRB members are appropriately knowledgeable in accordance with ethical standards and applicable regulations; for assuring the investigators are appropriately knowledgeable to conduct research in accordance with ethical standards and applicable regulations; and for the development and implementation of an educational plan for IRB members, staff, and investigators.

## Written policies and procedures

This Manual details the policies and regulations governing research with human participants. As the HRPP/IRB updates its policies and guidance, these documents will be posted to the HRPP website and will supersede relevant sections of this Manual where indicated.

The policies and procedures governing human subject research at Brown are reviewed regularly and may be revised by the Director, Office of Research Integrity, Associate Director of the HRPP, the Institutional Review Board, and University counsel, as necessary. The Vice President for Research, or those with delegated authority, will approve substantive revisions of the policies and procedures.

The Office of Research Integrity (ORI), Human Research Protection Program (HRPP) will keep the University research community apprised of new information that may affect the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues on its website and through campus electronic mailing lists. The policies and procedures will be available on the Brown University IRB website and copies will be available upon request.

## HRPP Organization

The HRPP is a program designed to ensure the protection of human participants in research. It consists of various individuals and committees such as: the Vice President for Research, the Associate Vice President for Research, the Office of Research Integrity, the IRB, other committees or subcommittees addressing human research protection (e.g., Biosafety, Radiation Safety, Conflict of Interest), investigators, research staff, and health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer.) The objective of this program is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human participants in research.

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

## Vice President for Research

As detailed above (*Institutional Official of the HRPP*), the ultimate responsibility of the HRPP resides with the Vice President for Research, who serves as the Institutional Official (IO) of the program. The responsibility for the HRPP at Brown University is delegated by the IO to the Director of the Office of Research Integrity.

## Senior Director, Office of Research Integrity

The Senior Director of the Office of Research Integrity (ORI Director) reports to the Associate Vice President for Research 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;
			2. Advising the VPR on key matters regarding research at Brown University;
			3. Implementing the institution’s HRPP Manual;
			4. Maintaining an approved FWA through the Vice President for Research and the Department of Health and Human Services Office for Human Research Protection (OHRP);
			5. Managing the finances of the Brown University HRPP;
			6. Assisting investigators in their efforts to carry out the University’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.

## Institutional Review Board (IRB)

Brown University has one IRB, appointed by the Vice President for Research. The IRB prospectively reviews and makes decisions concerning all human research conducted by its employees or agents. The IRB discharges its duty by complying with the requirements of the Common Rule, state regulations, the FWA, and institutional policies.

## University Office of the General Counsel

The Brown University HRPP relies on the Office of the General Counsel for interpretations and applications of Rhode Island law and the laws of any other jurisdiction where research is conducted as they apply to human research.

## Relationship between Components

The IRB functions independent of, but in coordination with, other institutional regulatory committees. The IRB makes independent determinations of whether to approve or disapprove a protocol based upon whether or not human participants are adequately protected. The IRB has review jurisdiction over all research involving human participants conducted, supported, or otherwise subject to regulation, by any federal department or agency that has adopted the human research regulations.

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of the institution. However, those officials may NOT approve research if it has been disapproved by the IRB.

## HRPP Office

The Brown University HRPP office, known as the Human Research Protection Program (HRPP), is part of the Office of Research Integrity (ORI), reports directly to the Associate VPR and is supervised by the Associate Director, HRPP. The Associate Director has expert knowledge in regulatory issues regarding human research protections and is the primary contact at Brown University for the Office for Human Research Protections, Department of Health and Human Services.

The Associate Director, HRPP has day-to-day responsibilities for the operation of the HRPP. This includes responding to faculty, student, and staff questions about human research as well as organizing and documenting the review process. The Associate Director works closely with the Chair of the IRB in the development of policy and procedures and is a voting member of the IRB. Additionally, the office is staffed by managers and specialists. The duties and responsibilities for all staff are found in their respective job descriptions, and their performance is evaluated on an annual basis.

## 1.11.2 HRPP Resources

The HRPP is equipped with 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 regularly by the ORI Director with the Associate Director, HRPP. The IO provides resources to the IRB and HRPP, including adequate meeting and office space and staff for conducting IRB business.

## 1.12 Non-University Institutional Audits and Compliance Reviews

External directed (“for cause”) audits and compliance reviews may be conducted at non- University sites, where the University’s IRB serves as the “IRB of Record” to assess compliance with federal, state, and local law; participant safety; and IRB policies and procedures. These directed audits are implemented in response to identified concerns that require an IRB determination.

## 1.13 Collaborative Research Projects

In the conduct of collaborative research projects, Brown University acknowledges that each institution is responsible for safeguarding the rights and welfare of research participants and for complying with applicable federal regulations and institutional policies. Brown University may enter into a joint review arrangement or rely on the review of another IRB, ethics committee, or any institution with a Federalwide Assurance (FWA).

If a multi-site study involving non-exempt human subjects research is funded by the National Institutes of Health (NIH) via a grant or contract submitted to the NIH on or after January 25, 2018, then the NIH single IRB (sIRB) policy requires the use of a single IRB to accomplish IRB review and approval for all domestic sites.

 The NIH policy applies to all studies that are:

* Funded through grants, cooperative agreements, or contracts and
* Involve non-exempt human subjects research, and
* Involve multiple domestic sites, all of which are conducting the same protocol

The policy does not apply to studies that are:

* Funded to foreign awardees and/or conducted at foreign sites, or
* Funded through career development, research training or fellowship awards, or
* Where review by the proposed sIRB would be prohibited by a federal, tribal, or state law, regulation, or policy.

A formal relationship must be established between the University and the other institution(s) through either a Cooperative Agreement, a Memorandum of Understanding, or an IRB Authorization Agreement (IAA). This relationship must be formalized before the University will accept any human research proposals from the other institution or rely on the review of the other institution.

For collaborative research, 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 Brown University relies on another IRB, the HRPP staff will ensure that the other organization has an active Assurance and appropriate policies in place.
* When Brown University 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 Brown University IRB or (ii) through subsequent review by appropriate designated institutional officials, such as the Chairperson and/or other IRB members.

The 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 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 investigator is responsible for ensuring that the research study is reviewed and approved by any other appropriate committees at the collaborating facility and at the participating facilities prior to enrollment of participants.

# IRB Review Process

## Purpose

The following describe the procedures required for the review of research by the IRB.

## 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 participants
		2. the research design or methodology (adding procedures that are not eligible for expedited review would not be considered a minor change)
		3. the qualifications of the research team
		4. the facilities available to support safe conduct of the research
		5. 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 temporarily stop some or all previously approved research activities. Suspended protocols remain open and require continuing review.

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

## Human Subjects Research Determination

The responsibility for initial determination of whether an activity constitutes human subjects research and therefore requires a submission to the HRPP/IRB rests with the Investigator. The Investigator should make this determination based on the guidance provided by the Brown HRPP on its website and the embedded assessments in the submission Applications.

## Exempt Studies

 Certain categories of research do not require IRB review and approval. Exempt research determinations that do not require Limited IRB Review are conducted by the HRPP team. Limited IRB review is a process that is required only for certain exemptions, and does not require an IRB to consider all of the IRB approval criteria in §46.111. In Limited IRB Review, the IRB must determine that certain conditions, which are specified in the regulations, are met. Limited IRB review may be done via the expedited review mechanism, that is, by the Chair or an experienced IRB member (or by the convened IRB, if requested).

Research that is determined to be Exempt has no expiration date; however, Investigators are required to inform the HRPP when an Exempt study has ended and to cooperate in any compliance monitoring conducted by the ORI’s Quality Assurance/Quality Improvement (QA/QI Program) or any other inquiries or investigations.

## Categories of Exempt Research

## The following types of studies do not qualify as exempt research:

## Studies that involve the use of any FDA-regulated drugs, substances, biologics or devices;

## Studies that involve the use of ionizing radiation (e.g., X-ray, DEXA scan, etc.)

## Studies that involve the use of genetic information or tests;

## Studies that propose to study prisoners as a targeted population;

## Studies that involve linkage of personally identifiable data

Unless otherwise required by law or by a study sponsor or funding agency, research activities in which the only involving of human participants will be in or more of the following categories will qualify for exemption:

(1) Research, conducted in established or commonly accepted educational settings that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2) Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

(i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).

(3)(i) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

(A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(B) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(C) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).

(ii) For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

(iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

(4) Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of “health care operations” or “research” as those terms are defined at 45 CFR 164.501 or for “public health activities and purposes” as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for non-research activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

(5) Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

(i) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

(6) Taste and food quality evaluation and consumer acceptance studies:

(i) If wholesome foods without additives are consumed, or

(ii) 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.

(7) Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by §46.111(a)(8).

(8) Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

(i) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with §46.116(a)(1) through (4), (a)(6), and (d);

(ii) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with §46.117;

(iii) An IRB conducts a limited IRB review and makes the determination required by §46.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph (d)(8)(i) of this section; and (iv) The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.

## 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)]
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)]

## 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. The HRPP team member making the determination of exemption will determine whether to require additional protections for participants in keeping with the guidelines of the Belmont Report.

## Expedited Review

Expedited review at Brown is conducted by an experienced IRB member. The IRB member conducting the expedited review may exercise all of the authorities of the IRB, except that the reviewer may not disapprove the research. The reviewer must refer any research protocol that he/she would have disapproved to the Full IRB for review. The reviewer may also refer other research protocols to the Full IRB whenever the reviewer believes that Full IRB review is warranted.

A) Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the below categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed 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.

B) The categories apply regardless of the age of subjects, except as noted.

C) 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.

D) The expedited review procedure may not be used for classified research involving human subjects. Brown does not permit the conduct of classified research.

E)  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.

#### **Categories of Review**

**Category 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); or

(b) Research on medical devices for which (i) an investigational device exemption application (21CFR812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is bei ng used in accordance with its cleared/approved labeling.

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

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

(b) from other adults and children, considering the age, weight, and health of the participants, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these participants, 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.

**Category 3:** Prospective collection of biological specimens for research purposes by noninvasive means. Examples include:

(a) hair and nail clippings in a non-disfiguring 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.

**Category 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 include:

(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.

**Category 5:**Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human research participants. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

**Category 6:** Collection of data from voice, video, digital, or image recordings made for research purposes.

**Category 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 HHS regulations for the protection of human research participants. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

**Category 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 participants;

                        (ii) all participants have completed all research-related interventions; and

                        (iii) the research remains active only for long-term follow-up of participants; or

            (b) where no participants have been enrolled and no additional risks have been identified; or

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

**Category 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.

## Informing the IRB

IRB members will be apprised of all expedited review approvals by means of a list in the meeting agenda. Any IRB member can request to review the full application for a study reviewed via expedited procedures by contacting the HRPP.

## Preliminary Review & Assignment to convened IRB Meeting

Investigators must submit an application found on the HRPP website electronically to the HRPP via the email IRB@Brown.edu. Each application contains an embedded assessment to facilitate the Investigator’s submission of the type of application (e.g., Exempt vs. Full Board/Expedited) most appropriate for the research.

HRPP staff will perform a preliminary review of the application to ensure it contains all required components and associated documents. Only complete submissions will undergo a formal review by the HRPP or IRB. Deadlines for application submissions for Full Board review are posted on the HRPP website; applications of appropriate quality that contain all required components received by the stated deadline will be reviewed by the IRB at its next convened meeting. Applications that meet expedited review criteria or exempt criteria are reviewed on a rolling basis based on the submission date.

Applications for research associated with a Just-in-Time or other sponsor request that contains an explicit deadline will receive a priority review. Investigators must submit to the HRPP the correspondence from the sponsor that reflects the deadline for IRB approval. When submitting an application for research that has an impending funding deadline, the Investigator should note this in the subject line of the email sent to the HRPP accompanying the application.

## Assignment and conduct of reviews

Full Board review

After it has been determined that the protocol submission is complete and meets criteria for review at a convened IRB meeting, HRPP staff, with the assistance of the IRB Chair, as necessary, will assign protocols for review paying close attention to the scientific content of the protocol and the potential reviewer’s area of expertise. At least one reviewer will be assigned to each protocol. Reviewers are assigned to all protocols requiring initial review and to all modifications. When the IRB is presented with a protocol which may be outside of the knowledge base of any of the IRB members, an outside consultant will be sought.

Primary reviewers are responsible for:

1. having a thorough knowledge of all of the details of the proposed research; and
2. performing an in-depth review of the proposed research; and
3. leading the discussion of the proposed research at the convened meeting and leading the IRB through the regulatory criteria for approval; and
4. making suggestions for changes to the proposed research in accordance with regulatory criteria, where applicable.

If the primary reviewer is absent from the meeting, a new reviewer may be assigned, provided the new reviewer has reviewed 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 IRB members receive, and are expected to review, the entire protocol package for all studies, not just the ones to which they are assigned as reviewers.

Expedited and Limited IRB Review

Research that meets criteria for expedited and/or Limited IRB Review is conducted by a qualified IRB member. Frequently the reviewer is an IRB member who is also a member of the HRPP team.

## Quorum

A quorum for the purpose of a convened IRB meeting 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. If research involving prisoners is reviewed, Brown’s prisoner representative 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 to ensure that the meetings remain appropriately convened.

A quorum must be maintained for each vote to occur. HRPP 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 protocol must be deferred or the meeting must be terminated.

Members are considered present and counted towards the quorum 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.

Opinions of absent members that are transmitted in written form may be considered by the attending IRB members but may not be counted as votes or to satisfy the quorum for convened meetings.

## Guests

When an Investigator’s application is being reviewed at a convened IRB meeting, the Investigator is invited to attend the IRB meeting and/or remain available via phone to answer questions about the proposed research. The PI may not be present for the discussion or vote on their own research.

Other guests may be permitted to attend IRB meetings at the discretion of the IRB Chair and the HRPP Associate Director and/or ORI Director. Guests may not speak unless requested by the IRB and are required to sign a Confidentiality Agreement.

##

## Criteria for IRB Approval of Research

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

1. Risks to participants are minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose participants to risk, and (ii) whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.
2. Risks to participants are reasonable in relation to anticipated benefits, if any, to participants, and the importance of the knowledge that may reasonably be expected to result. 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 participants 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 participants 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.
4. Informed consent will be sought from each prospective participant or the participant'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 participants.
7. When appropriate, there are adequate provisions to protect the privacy of participants and to maintain the confidentiality of data.
8. When some or all of the participants are likely to be vulnerable to coercion or undue influence, such as children, prisoners, 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 participants.

## Risk/Benefit Assessment

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

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

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

1. identify the risks associated with the research, as distinguished from other risks, such as the risks of therapies the participants 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 participants, if any, and assess the importance of the knowledge to be gained;
5. ensure that potential participants will be provided with an accurate and fair description of the risks or discomforts and the anticipated benefits.

Risks to participants are minimized:

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

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

1. 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 participants would receive even if not participating in the research.
2. 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.

## Research Design

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

* + - * 1. The research uses procedures consistent with sound research design;
				2. The research design is sound enough to reasonably expect the research to answer its proposed question; and
				3. 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.

## Selection of participants is equitable

The IRB determines by viewing the application and associated documents that the selection of participants is equitable with respect to sex, age, class, etc. The IRB will not approve a study that does not provide adequately for the equitable selection of participants 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 purpose(s) of the research;
* the setting in which the research occurs;
* scientific and ethical justification for including vulnerable populations;
* the scientific and ethical justification for excluding classes of persons who might benefit from the research; and
* the inclusion/exclusion criteria.

## Recruitment of Participants

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

## Informed Consent / Parental permission / Child assent

The IRB will ensure that informed consent will be sought from each prospective participant or the participant’s legally authorized representative. In research involving minor children, assent of the child and parental permission will be sought, as appropriate. The IRB will further ensure that consent is documented or otherwise approve, as appropriate, a waiver of documentation of consent.

## Data Safety Monitoring

The IRB determines that, where appropriate, the research plan makes adequate provision for monitoring the data to ensure the safety of participants. For research in which risks are substantial, the IRB may require a general description of the data and safety monitoring plan to be submitted to the IRB as part of the application. This plan should contain procedures for reporting incidents that meet criteria set forth in Brown’s *Reportable Events Policy*. In general, it is desirable for a Data and Safety Monitoring Board (DSMB) to be established by the study sponsor for research that is blinded, involves multiple sites, involves vulnerable participants, 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 where 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 reviewed, 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.

## Privacy and Confidentiality

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

Privacy is the control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. The evaluation of privacy also involves consideration of how the researcher accesses information from or about potential participants (e.g., recruitment process). IRB members consider strategies to protect privacy interests relating to contact with potential participants, and access to private information.

Confidentiality pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure. During the informed consent process, if applicable, subjects must be informed of the precautions that will be taken to protect the confidentiality of the data and be informed of the parties who will or may have access (e.g., research team, FDA, OHRP). This will allow subjects to decide about the adequacy of the protections and the acceptability of the possible release of private information to the interested parties.

At the time of initial review, the IRB assesses whether there are adequate provisions to protect participant privacy and maintain confidentiality. The IRB does this through the evaluation of the:

* + - * 1. methods used to obtain information about participants;
				2. methods used to obtain information about individuals who may be recruited to participate in studies;
				3. the use of personally identifiable records; and
				4. the methods to protect the confidentiality of research data.

## Vulnerable Populations

At the time of initial review the IRB will consider the scientific and ethical reasons for including vulnerable participants in research. The IRB may determine and require that, when appropriate, additional safeguards are put into place for vulnerable participants.

In accordance with the federal regulations, vulnerable participants are individuals “vulnerable to coercion and undue influence, in recognition that coercion or undue influence refers to the ability to make an informed decision about participating in research.” Inclusive in this definition are individuals with impaired decision-making capacity, prisoners, and children.

The IRB carefully considers group characteristics, such as economic, social, physical, and environmental conditions, to ensure that the research incorporates additional safeguards for vulnerable participants.

## Additional Considerations during IRB Review and Approval of Research

## Determination of Risk

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

## Period of Approval

At the time of initial review and at continuing review, when applicable, 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 (unless the research has progressed to the point that it meets criteria set forth in the Continuing Review section, below). In some circumstances, a shorter review interval (e.g. biannually, quarterly, or after accrual of a specific number of participants) may be required. The meeting minutes will reflect the IRB’s determination regarding review frequency.

## Review More Often than Annually

Research that meets any of the following criteria may require review more often than annually:

* + - * 1. significant risk to research participants (e.g., death, permanent or long lasting disability or morbidity, severe toxicity) without the possibility of direct benefit to the participants;
				2. the involvement of especially vulnerable populations likely to be subject to coercion (e.g., terminally ill)
				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. probability and magnitude of anticipated risks to participants.
2. likely medical condition of the proposed participants.
3. overall qualifications of the PI and other members of the research team.
4. specific experience of the PI and other members of the research team in ­­conducting similar research, nature and frequency of adverse events observed in similar research at this and other institutions.
5. novelty of the research making unanticipated adverse events more likely.
6. 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 participants either studied or enrolled. If a maximum number of participants studied or enrolled is used to define the approval period, it is understood that the approval period in no case can exceed one year and that the number of participants studied or enrolled determines the approval period only when that number of participants is studied or enrolled in less than one year.

## Investigator Conflicts of Interest (COI)

Brown’s IRB is dedicated to upholding the highest ethical standards of objectivity in research by identifying and evaluating financial conflicts of interest (FCOI) that may affect an individuals’ decision to participate in the research based on any perceived or actual risks associated with the FCOI.

As part of the application for IRB review, the Brown IRB requires Investigators to:

* certify that they have submitted a COI Assurance or COI Reporting Form within the last 12 months and that it is up-to-date; and
* identify if any of their reported significant financial interests are related to the proposed human subject research protocol conducted at Brown or using Brown resources (i.e., Brown funding, facilities).

For purposes of disclosure to the IRB, an Investigator means the project director or principal investigator and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research, which may include, for example, postdoctoral fellows, collaborators, or consultants.

A Brown Investigator means anyone working on a human subject study protocol that meets the above definition of an Investigator and is either appointed by or employed by Brown (and, therefore, must abide by Brown’s [Conflict of Interest Policy for Officers of Instruction and Research](https://www.brown.edu/research/COIpolicy) [Brown’s COI in Research Policy]). A Brown Investigator also means anyone working on a human subject study protocol that meets the above definition of an Investigatorand does not have a compliant COI policy at his/her home institution that he/she must follow, and, therefore, must follow Brown’s COI Policy.

Related financial interests occur when the researcher, spouse or registered domestic partner, or dependent children, have a disclosable financial interest that 1) would reasonably appear to be affected by the research; or 2) when the entity in which the financial interests are held would reasonably appear to be affected by the research.

The Office of Research Integrity coordinates COI review. Related financial interests disclosed through the IRB process will either have already been reviewed by the COI Review Board, or will be referred to COI administrators for assessment. Similarly, if the COI Review Board is prompted to review a human subject Investigator’s significant financial interest(s) reported either through the Annual COI Assurance process or via a transactional COI Reporting Form, the COI Review Board will provide relevant information to the IRB for its consideration.

The IRB will evaluate whether a disclosure in the informed consent form (or other actions) are necessary. If disclosure is required and the Investigator has not already included [recommended disclosure language](https://www.brown.edu/research/sites/research/files/COI%20IRB%20consent%20language%20%2829Jan18%29%20FINAL.pdf) in the informed consent, then the IRB will specify acceptable language. When a financial interest may affect the protection of human subjects, disclosure to potential human subjects and/or the public may not be a sufficient method of management of the conflict of interest. In such an instance, the COI Review Board and/or the IRB might recommend or require a limited role of certain researchers with financial interests to recruit or consent subjects or to analyze data.

## Significant New Findings

During the course of research, significant new knowledge or findings about the topic 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 participants’ rights and welfare. Since the new knowledge or findings may affect the risks or benefits to participants or participants' willingness to continue in the research, the IRB may require, during the ongoing review process, that the PI contact the currently enrolled participants to inform them of the new information. The IRB will communicate this to the PI. The informed consent should be updated and the IRB may require that the currently enrolled participants be re-consented, acknowledging receipt of this new information and for affirming their continued participation.

## Payment to Research Participants

Payment to research participants may be an incentive for participation or a way to reimburse a participant 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 take care to avoid coercion of participants.

Payments should reflect the degree of risk, inconvenience, or discomfort associated with participation. The amount of compensation must be proportional to the risks and inconveniences posed by participation in the study.

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

* + - 1. substantiate that proposed payments are reasonable and commensurate with the expected contributions of the participant;
			2. state the terms of the participation agreement and the amount of payment in the informed consent form; and

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

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

Credit for payment should accrue and not be contingent upon the participant completing the entire study. Whenever possible, 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 participants would receive partial payment or no payment (e.g., if they withdraw from the study before their participation is completed).

## Compliance with all Applicable State and Local Laws

The IRB follows and must adhere to all applicable state and local laws in the jurisdictions where the research is taking place. The HRPP and the IRB rely on the University Counsel for the interpretation and application of State law and the laws of any other jurisdiction where research is conducted as they apply to human research.

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

## Possible IRB Actions

The following are possible actions the IRB can take after reviewing a research application.

Approved: An IRB action taken when the required determinations are made that allows research involving human subjects to proceed consistent with federal regulations, state and local laws, and University policy.

Modifications Required: An IRB action that specifies conditions under which research can be approved, pending the following:

* Confirmation of specific understandings by the IRB about how the research will be conducted, submission of additional documentation, precise language changes to the protocol and/or informed consent document(s), and/or substantive changes to documents with specific parameters the changes must satisfy.
* Verification that the investigator’s response(s) satisfies the conditions for approval set by the IRB may be performed by the IRB Chair and/or other designated individual(s). Also referred to as: contingent approval, approval with conditions.

Deferred: An IRB action taken when the convened IRB cannot fully evaluate the research under review and make the determinations required for approval without modifications to the protocol and/or informed consent document, or submission of clarifications or additional materials prior to reconsideration of the research. Convened IRB review of the investigator’s response(s) is required.

Disapproved: An IRB action taken when the determinations required for approval of research cannot be made, even with substantive clarifications or modifications to the protocol and/or informed consent process/document. Research cannot be disapproved by expedited review.

Tabled: An IRB “action” that indicates that review was not initiated or was not completed, resulting in postponement of IRB review, usually due to loss of quorum or other administrative issue. Research tabled at a convened meeting will be reviewed at a future convened meeting.

## Continuing Review

Continuing review of approved research is not required for:

1. Research that is eligible for expedited review;
2. Exempt research conditioned on limited IRB review;
3. Research that has completed all interventions and now only includes analyzing data, even if the information or biospecimens are identifiable;
4. Research that has completed all interventions and now only includes accessing follow-up clinical data from clinical care procedures.

The Brown IRB can choose to require continuing review for the above-referenced research, as long as the IRB documents the decision and the rationale for this decision.

Unless it meets criteria stipulated above, research that has undergone Full Board review and approval is subject to continuing review. FDA-regulated studies reviewed under expedited of Full Board review criteria are subject to continuing review.

## Lapse in Approval

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 within the timeframe set 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 participants 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.

The HRPP will promptly notify the investigator of the expiration of approval and that all research activities must stop. 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 a list of research participants for whom suspension of the research would cause harm. Enrollment of new participants cannot occur and continuation of research interventions or interactions for already enrolled participants should only continue when the IRB or IRB Chair finds that it is in the best interest of the individual participants to do so.

Failure to submit continuing review information on time is non-compliance and will be handled in accordance with Brown’s *Reportable Events Policy*.

If the study is FDA-regulated, the IRB Chair must follow FDA requirements in 21 CFR 56.108(b)(3) in making their decision.

The sponsoring agency, private sponsor, or other Federal agencies must be informed, as appropriate.

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 30 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 30 days or less and the PI provides the required continuing review information, the existing protocol may be reviewed for consideration of continued IRB approval.

If a research protocol receives contingent approval at the time of the continuing review and the approval expires before the PI responds to the contingencies, the PI may not enroll any new participants after the approval expiration date. 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 vote to 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.

## Amendment to an Approved Protocol

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

In order to obtain approval, investigators must submit an Amendment Request Form to the HRPP at IRB@Brown.edu.

HRPP staff will determine the appropriate level of review for the proposed changes. 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 amendment for Full Board review.

The requested changes must not be implemented until IRB approval has been granted, which will be communicate the Principal Investigator in writing.

## Reporting IRB Actions

All IRB actions are communicated to the PI, and/or designated primary contact person for the protocol, in writing by the HRPP staff. For an approval, written notification of approval will be sent. For a deferral, the notification will include the modifications required for approval along with the basis for requiring those modifications. For a disapproval, termination or suspension, the notification will include the basis for making that decision. The IRB reports its findings and actions to the University in the form of its minutes which are stored permanently and securely in the HRPP Office. Copies of minutes are distributed by HRPP staff to the Brown University Institutional Official (IO).

##

## Appeal of IRB Decisions

When research presented at a convened meeting of the IRB is disapproved, deferred or requires 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 person or 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 recommendations for approval remain under the purview of the IRB.

# Documentation and Records

## 3.1 IRB Records

The IRB must prepare and maintain adequate documentation of the IRB’s activities including, copies of all items reviewed, including, but not limited to:

* + 1. research applications
		2. investigators’ brochures, if any
		3. recruitment materials
		4. scientific evaluations (if any) that accompany the proposals
		5. approved consent documents, including DHHS-approved sample consent document and protocol, when they exist
		6. HIPAA Authorization documents if separate from the informed consent documents
		7. records of continuing review activities, including progress reports submitted by investigators
		8. any proposed amendments and the IRB action on each amendment
		9. reports of injuries to participants and serious and unexpected adverse events
		10. documentation of protocol violations
		11. documentation of non-compliance with applicable regulations
		12. statements of significant new findings provided to participants
		13. IRB membership roster(s)
		14. IRB meeting minutes
		15. Copies of all correspondence between the IRB and the investigator

IRB records must also document any determinations required by the regulations and protocol-specific findings supporting those determinations, including:

* + 1. waiver or alteration of the consent process
		2. research involving pregnant women, fetuses, and neonates
		3. research involving prisoners
		4. research involving children

## 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 university)
4. Status as scientist (physician-scientist, other scientist, non-scientist or social behavioral scientist). For purposes of this roster, IRB members with research experience are designated as scientists (including the student member). Research experience includes training in research (e.g., doctoral degrees with a research-based thesis) and previous or current conduct of research. Students being trained in research fields will be 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. Voting status (Any *ex officio* members are non-voting members)
9. Alternate status, including the member they alternate with
10. Relationship (e.g., employment) between the individual IRB member and the organization

The HRPP must keep the IRB membership list current.

## IRB Minutes

Proceedings should be written and available for review by the next regularly scheduled IRB meeting date. Once approved by the IRB at a subsequent IRB meeting, the minutes must not be altered by anyone.

Minutes of IRB meetings must contain sufficient detail to show:

1. Attendance
	1. names of members present
	2. 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
	3. names of absent members
	4. names of alternates attending in lieu of specified (named) absent members. (Alternates may substitute for specific absent members only as designated on the official IRB membership roster)
	5. names of consultants present
	6. name of investigators present
	7. names of guests present

The initial attendance list shall include those members present at any point during the meeting. The minutes will indicate, by name, those members who enter or leave the meeting. The vote on each action will reflect the number of members present for the vote on that item.

1. The presence of a quorum throughout the meeting, including the presence of one member whose primary concern is in a non-scientific area
2. Business Items discussed
3. Continuing Education
4. Actions taken, including separate deliberations, actions, and votes for each protocol undergoing initial review, continuing review, or review of modifications by the convened IRB
5. Votes on these actions (total number voting; number voting for; number voting against; number abstaining; number of those excused; number of those recused)
6. Basis or justification for these actions including required changes in research
7. Summary of controverted issues and their resolution
8. Approval period for initial and continuing approved protocols, assumed to be 12 months unless otherwise indicated
9. Risk level of initial and continuing approved protocols
10. Review of interim reports, e.g. adverse event or safety reports, amendments, report of violation, etc.
11. Review of Data and Safety Monitoring Board (DSMB) summary
12. Applications that have met or not met requested stipulations
13. 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
14. Study-specific documentation that the research meets the required criteria [45 CFR 46.117(c)] when the requirements for documentation of consent are waived
15. 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.
16. Determination of the risk level of investigational devices and the rationale for such determinations
17. Determinations of conflict of interest.
18. 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 (e.g., Cooperative Studies, or other collaborative research).
19. Special protections warranted in specific research projects for groups of participants who 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, regardless of source of support for the research.
20. A list of research approved since the last meeting utilizing expedited review procedures and the specific citation for the category of expedited review of the individual protocol.
21. Documentation of approval by the Chair or designee of research contingent on specific minor conditions in the minutes of the first IRB meeting that takes place after the date of the approval.
22. An indication that, when an IRB member has a conflicting interest with the research under review, the IRB member was not present during the deliberations or voting on the proposal, and that the quorum was maintained.
23. 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 made available to the Institutional Official.

## Documentation of Exemptions

Documentation of verified exemptions consists of the reviewer’s citation of a specific exemption category and written concurrence that the activity described in the investigator’s request for exemption satisfies the conditions of the cited exemption category.

## Documentation of Expedited Reviews

IRB records for initial and continuing review by the expedited procedure must include: the specific permissible category, a description of action taken, if any, by the reviewer, and any determinations required by the regulations and study-specific findings supporting those determinations.

## Record Retention

The above detailed records must be stored securely by the HRPP and must be retained for at least three years. Records pertaining to approved research must be stored securely by the HRPP and must be retained for at least three years after completion of the research. IRB records not associated with research or for studies closed without participant enrollment will be retained at the facility for at least three years after closure.

After that time those records may be shredded or otherwise securely destroyed. All records must be accessible for inspection and copying by authorized representatives of the OHRP, FDA, sponsors, and other authorized entities at reasonable times and in a reasonable manner.

Records are maintained in locked file cabinets and/or locked offices within the HRPP office and/or on secure university servers and are available only to IRB members, HRPP staff, and senior officers, as necessary.

# Obtaining Informed Consent from Research Participants

## Purpose

The following procedures describe the requirements for obtaining and documenting consent from participants in research conducted under the auspices of Brown University.

## Definitions

*Legally Authorized Representative (LAR)*: An LAR is 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. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

*Legal guardian*: A person appointed by a court of appropriate jurisdiction.

## Informed Consent Process

Informed consent must be obtained under the following circumstances:

1. Informed consent may only be obtained from participants who have the legal and mental capacity to give consent. For participants without that capacity, consent must be obtained from a legal guardian or a legally authorized representative.
2. The informed consent process shall be sought under circumstances that provide the participant or LAR with sufficient opportunity to consider whether or not to participate.
3. The informed consent process shall be sought under circumstances that minimize the possibility of coercion or undue influence.
4. The informed consent information must be presented in language that is understandable to the participant or LAR. 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.
5. The informed consent process must give prospective subjects the information that a reasonable person would want to have in order to make an informed decision about whether to participate.
6. The information needs to be presented in sufficient detail and organized and presented in a way that facilitates an understanding of why one might, or might not, want to participate. The key information about the study must be provided at the beginning. This should include information about the purpose, the risks, the benefits, and alternatives, and explain to the person how to think about these pieces of information in terms of making a decision. It should be presented in a concise and focused manner.
7. For participants whose native language is not English, informed consent must be obtained in a language that is understandable to the participant (or the participant’s legally authorized representative). The IRB requires that informed consent conferences include a reliable translator when the prospective participant does not understand the language of the person who is obtaining consent.
8. The informed consent process may not include any exculpatory language through which the participant is made to waive, or appear to waive, any of the participant’s legal rights or through which the investigator, the sponsor, the University, or University employees or agents are released from liability for negligence, or appear to be so released.
9. The PI is responsible for insuring that each prospective participant is adequately informed about all aspects of the research and understands the information provided.

The IRB may approve a proposal for the investigator to obtain information or biospecimens to screen, recruit, or determine eligibility of prospective subjects for a research study without informed consent. This is applicable if (1) the information is obtained through oral or written communication with the subject or the subject’s legally authorized representative, or (2) identifiable private information or identifiable biospecimens are obtained by accessing records or stored identifiable biospecimens. This is consistent with the FDA regulations.

## Basic Elements of Informed Consent

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the participant'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 participant;
2. A description of any benefits to the participant 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 participant;
4. A statement describing the extent, if any, to which confidentiality of records identifying the participant 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 participant;
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 participant 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 participant is otherwise entitled, and the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled;
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 participant confidentiality;
10. Notice about whether participants' information or biospecimens collected as part of the current research might be stripped of identifiers and used for other research in the future. Consent forms must indicate either that information or biospecimens collected for the research might be stripped of identifiers and used in other research in the future, or that this will not occur. Note that this is only about future research use of information and biospecimens that will be stripped of identifiers.

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

1. A statement that the particular procedure or treatment may involve risks to the participant, which are currently unforeseeable.
2. A statement that if the participant is or becomes pregnant, the particular procedure or treatment may involve risks to the embryo or fetus, which are currently unforeseeable.
3. Anticipated circumstances under which the participant’s participation may be terminated by the investigator without regard to the participant’s consent.
4. Any additional costs to the participant that may result from participation in the research.
5. The consequences of a participant’s decision to withdraw from the research.
6. Procedures for orderly termination of participation by the participant.
7. A statement that significant new findings developed during the course of the research which may relate to the participant’s willingness to continue participation will be provided to the participant. The approximate number of participants involved in the study.
8. Notice to participants about possible commercial profit from the research, whether clinically relevant research results will be returned to the participants, and whether research activities will or might include whole genome sequencing.

## Documentation of Informed Consent

Informed consent must be documented by the use of a written consent form approved by the IRB unless a waiver of consent is approved.

1. Informed consent is documented by the use of a written consent form approved by the IRB and signed and dated by the participant or the participant's legally authorized representative at the time of consent.
2. A copy of the signed and dated consent form shall be given to the person signing the form.
3. The consent form may be either of the following:
	1. A written consent document that embodies the basic and required additional elements of informed consent. The consent form may be read to the participant or the participant's legally authorized representative, but the participant or representative must be given adequate opportunity to read it before it is signed; or
	2. A short form written consent document stating that the elements of informed consent have been presented orally to the participant or the participant's legally authorized representative.

When this method is used:

* there must be a witness to the oral presentation; and
* the IRB must approve a written summary of what is to be signed by the participant or representative; and
* the witness must sign both the short form and a copy of the summary; and
* the person actually obtaining consent must sign a copy of the summary; and
* a copy of the summary must be given to the participant or representative, in addition to a copy of the short form.

## Waiver of Informed Consent

The 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:

1. The research involves no more than minimal tangible or intangible risk to the participants;
2. The waiver or alteration will not adversely affect the rights and welfare of the participants;
3. The research could not practicably be carried out without the waiver or alteration; and
4. Whenever appropriate, the participants must be provided with additional pertinent information after participation.
5. For research with identifiable private information or identifiable biospecimens, the IRB must determine that the research could not practicably be carried out without using the information or biospecimens in an identifiable form.

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 waives the requirements to obtain informed consent, provided the IRB finds and documents that:

1. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
	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.
2. 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.

## Waiver of Documentation of Informed Consent

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all participants if it finds that:

1. The only record linking the participant and the research would be the consent document and the principle risk would be potential harm resulting from a breach of confidentiality, and the research is not FDA-regulated, or only record linking the participant and the research would be the consent document and the principle risk would be potential harm resulting from a breach of confidentiality; or
2. The research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context.

The IRB may waive the requirement for a signed informed consent form if the subjects are members of a distinct cultural group or community in which signing forms is not the norm, the research involves no more than minimal risk, and there is an alternative method for documenting that consent was obtained. The waiver of documentation can be applied to broad consent.

In cases in which the documentation requirement is waived, the IRB requires the investigator to provide in the application materials a written summary of the information to be communicated to the participant, and the IRB will consider whether to require the investigator to provide participants with a written statement regarding the research.

# FDA Regulation Research

## Purpose

The following procedures describe the use of investigational drugs and devices in research under the auspices of Brown University. Use of investigational drugs must be conducted according to FDA IND regulations, 21CFR Part 312, and other applicable FDA regulations. Use of an investigational device to obtain safety and effectiveness data must be conducted according to FDA’s IDE regulations, 21CFR Part 812, and other applicable FDA regulations.

## Definitions

 ***Biological product****:* A virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound) applicable to the prevention, treatment, or cure of a disease or condition of human beings.

 ***Device:***An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory that is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease; or intended to affect the structure or any function of the body; AND which does not achieve its primary intended purposes through chemical action within or on the body and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

 ***Drug:***Articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease and articles (other than food) intended to affect the structure or any function of the body.

***Investigational Drug:***An investigational drug for clinical research use is one for which the PI or a sponsor has filed an IND application (21CFR 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:*** 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 21CFR Part 312.

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

*Emergency Use.* Emergency use is defined as the use of an investigational drug or biological product with a human participant 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):***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 participant; 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 participant; 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 participant; or
		4. Otherwise presents a potential for serious risk to the health, safety, or welfare of a participant.

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

***Humanitarian Use Device (HUD):***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.

## 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. [21CFR §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. [21CFR §56.104(d)]

## IND/IDE Requirements

When the principal intent of the investigational use of a test article is to develop information about the product’s safety or efficacy, an Investigational New Drug (IND) or Investigational Device Exemption (IDE) may be required.

If the protocol involves investigational drugs or devices, the investigator will be asked if there is an IND/IDE for the research and document assurances 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

If the research involves drugs or devices and there is no IND/IDE, the investigator will be asked for a rationale as to why it is not required.

For drugs, an IND may not be necessary if all seven of the following conditions are met:

1. The drug being used in the research is lawfully marketed in the United States;
2. 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;
3. The research is not intended to support a significant change in the advertising for the product;
4. The research does not involve a route of administration or dosage level, use in a participant population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
5. The research is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively];
6. The research is conducted in compliance with the requirements concerning the promotion and sale of drugs [21 CFR 312.7];
7. The research does not intend to invoke 21 CFR 50.24 (Exception from informed consent requirements for emergency research).

For devices, an IDE may not be necessary if:

1. There is a claim that it is a Non-significant risk device (NSR);
2. The research involves a device when used or investigated in accordance with the indications in labeling in effect at that time;
3. The research involves a device 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;
4. The research involves a diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:
	1. Is noninvasive,
	2. Does not require an invasive sampling procedure that presents significant risk,
	3. Does not by design or intention introduce energy into a participant, and
	4. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure;
5. 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 participants at risk;
6. The research involves a device intended solely for veterinary use;
7. The research involves a device shipped solely for research on or with laboratory animals and labeled in accordance with 21 CFR 812.5(c);
8. 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.

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 there are drugs or devices involved, but no IND/IDE, whether the research meets the above criteria.

## Responsibilities

## 5.5.1 Investigator

* + - * 1. The investigator is responsible for ensuring that the research is conducted according to all regulatory guidelines and must obtain approval from the Brown University IRB.
				2. The investigator proposing the drug/device research will be required to provide a plan, that will be evaluated by the IRB, that will include: (a) storage, (b) security,
1. dispensing.
	* + - 1. The investigator is responsible for the investigational drug/device accountability which includes storage, security, dispensing, administration, return, disposition and records of accountability. The investigator will delegate the responsibility for drugs/biologic accountability to the pharmacy service.
				2. If, because of special circumstances, an investigational drug/device is not stored in the pharmacy, the investigator is responsible for the storage, security and dispensing of the drug/device. The investigator must complete and submit an investigational control sheet containing information on the plan for storage, security and dispensing of the drug/device to the IRB prior to its approval of the study. 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 investigator’s control. Proper instructions on the use of the drug/device must be provided to the participants. A log must be kept regarding the receipt, use and/or dispensing of the drug/device and the disposition of remaining devices at the conclusion of the investigation.
				3. The investigator shall report all unanticipated problems involving risk to participants or others to the IRB in accordance with the Brown HRPP *Reportable Events Policy*.
				4. For research involving investigational new drugs:
2. The PI is responsible for informing the pharmacy service that IRB approval has been obtained. In addition a signed copy, of the consent form must be sent to pharmacy service to document each participant’s consent to participate in the study.
3. The PI must inform the pharmacy service when a study involving investigational drugs has been terminated.
4. The investigator shall report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug according to the procedures in the protocol.
	* + - 1. For research involving investigational devices:
5. If a device considered NSR by the investigator or sponsor, is determined to have significant risk upon IRB review, the investigator is responsible for notifying the sponsor of the IRB’s determination upon receipt of written notice. The PI should provide the IRB with confirmation of this action.
6. A copy of the protocol approval by the FDA and the IRB and the consent must be provided to the pharmacist if the device will be stored in the pharmacy. A request for the IDE and a copy of the signed consent from the research participant must be provided to the pharmacist when the device is required for use. If the investigator is storing the devices, a log must be maintained to indicate name of participant, date dispensed, by whom it was dispensed, amount remaining, and who received the device.
7. The investigator shall 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.
	* + - 1. Following completion of the study, the termination procedure for investigational drugs must be applied if under pharmacy control. If the devices are kept by the investigator, the log must be completed regarding the receipt, use and/or dispensing of the device, and the disposition of remaining devices at the conclusion of the investigation.
				2. When an investigator files an IND or IDE, the investigator is considered the sponsor and as such carries all of the FDA regulatory responsibilities and reporting obligations of both the Investigator and sponsor as described in the FDA regulations. The investigator will affirm that they are aware of and will comply with the regulatory responsibilities of a sponsor.

## IRB

* + - * 1. The IRB must review the research in accordance with these requirements and needs to use 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:
1. The IRB is responsible for reviewing the protocol and determining if the device represents significant risk (SR) or non-significant risk (NSR) and report the findings to the investigator in writing. The IRB must 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. If a study that has been submitted as NSR is considered SR, the IRB must recommend that an IDE be obtained.
2. Protocols involving significant risk devices do not qualify for expedited review.

The IRB must document in the Minutes the rationale for the determination of a device that is classified as NSR/SR.

1. The IRB will provide written documentation of approval to the investigator with a determination of whether the device presents a significant or non-significant risk.

## Emergency Use

## Emergency Exemption from Prospective IRB Approval.

FDA defines emergency use as the use of an investigational drug or biological product with a human participant 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 is required unless the conditions for exemption are met. The IRB must be notified within 5 working days when an emergency exemption is used. Any subsequent use of the test article at the institution is subject to IRB review.

If the PI notified the IRB prior to the emergency use of an investigational test article, the circumstances will be reviewed by IRB staff to determine that it meets FDA regulations and the investigator will be advised accordingly. All after-the-fact reports to the IRB of emergency use will be reviewed by IRB staff to determine the circumstances and for compliance with FDA regulations.

## Emergency 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:

1. The participant is confronted by a life-threatening situation necessitating the use of the test article;
2. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the participant;
3. Time is not sufficient to obtain consent form the participant’s legally authorized representative;
4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the participant’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 5-6 working days. The emergency use must be reported to the IRB within 5 working days. This reporting must not be construed as an approval for the emergency use by the IRB.

## Treatment IND

FDA regulations (21 CFR 312.34 and 312.35) address the treatment use of an investigational drug (not approved for marketing, but under clinical investigation for a serious or immediately life-threatening disease condition) in patients for whom no comparable or satisfactory alternative drug or other therapy is available. Use of the investigational drug for this purpose must meet all applicable FDA requirements.

## 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.

## 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).

## Humanitarian Use Devices (HUD)

In accordance with 21 CFR 814.124, treatment with a HUD is subject to full board initial and continuing review by the IRB. At the time of review, the IRB will determine if written consent from participants for use of the HUD is necessary. If a physician in an emergency situation determines that IRB approval cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be administered without prior IRB approval. In this instance, approval must be obtained from the appropriate local authority (such as the Chief of Staff), and the investigator is required to provide written notification of the use to the IRB within five days after use of the device. The IRB requires that written notification include identification of the patient, the date on which the device was used, and the reason for the use. It is the responsibility of the investigator to notify the FDA if the IRB were ever to withdraw approval for use of a HUD. The FDA should be notified within five days of notification of the withdrawal of approval. Investigators are reminded that Humanitarian Device Exemptions are for clinical use only and HUDs can be used only for purposes outlined in the approved IRB application.

# Special Topics

## Mandatory Reporting

While any person may make a report if they have reasonable cause to believe that a child or elder was abused or neglected, Rhode Island law mandates that certain persons who suspect child or elder abuse or neglect report this to the appropriate State agencies.

In situations where conditions of abuse or neglect might be revealed, mandated reporters should make themselves known as such to parents of children under age 18, to participants who are children, and to participants who are potential victims of abuse or neglect.

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