Subject: Human Research Protections Program

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POLICY AND PURPOSE

This policy manual includes procedures to be followed in the preparation and submission of research protocols, including informed consent documents, for review by the State University of New York (SUNY) Downstate Medical Center (DMC) Institutional Review Board (IRB). It also includes information on the responsibilities of investigators and key personnel during the conduct of human research and after a study is closed.

This policy helps to ensure compliance with the terms of a Federal Wide Assurance (FWA00003624) with the US Department of Health and Human Services, Office for Human Research Protections (OHRP). This assurance applies to all human research conducted by anyone on the premises of DMC and to research conducted elsewhere by workforce in connection with their institutional responsibilities.

This policy ensures compliance with all policies, regulations, and laws pertaining to human research, including the requirements of the local jurisdiction where research takes place or the local jurisdiction where specimens or data are derived.

All activities which require IRB review must have IRB approval and meet other applicable requirements before they begin. Any IRB, including the DMC IRB committees or external IRBs, with review and oversight of DMC must be registered with OHRP. The DMC IRB Committees (A, B, & E) are registered with OHRP and designated as the primary IRB that reviews the most research.

DMC complies with 45 CFR 46 (The Common Rule) and must follow FDA regulations (21 CFR 50, 56, 312, 812) for clinical trials and device studies. When required by the sponsor, investigators must follow the principles of Good Clinical Practices when conducting clinical trials. DMC complies with the requirements of other Federal Departments or Agencies, when they fund or support a research project. When the research involves Protected Health Information, DMC must comply with the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The IRB and investigators must comply with this policy and all other applicable DMC policies pertaining to research, including those of the DMC Office of Compliance and Audit Services (OCAS). Principal Investigators (PI) and investigators for the purposes of conflict of interest (COI), as determined by the PI, must follow the NIH regulations on financial Conflicts of Interest, as outlined in DMC Conflict of Interest Policy. A list of regulations, which may be applicable to certain research, as determined by the IRB are provided in the reference section of this policy.

**NOTE:** The U.S. Department of Health and Human Services and fifteen other Federal Departments and Agencies’ published revisions to the Federal Policy for the Protection of Human Subjects (the Common Rule) on January 19, 2017. These revisions are an effort to modernize, simplify, and enhance the current system of oversight. The Final Rule and additional related information can be accessed at:
Investigators and key personal from external sites that are approved to conduct research by the DMC IRB, must follow both DMC policy and the policies of their own institution.

When regulations or policies are in conflict with one another, DMC abides by the most stringent rule to allow the most protection to research participants and maintain regulatory compliance. Investigators who face a conflict about which regulation or policy to apply are directed to consult with the IRB to make a determination on how to proceed.

Copies of any referenced documents or forms are available on the Office of research Administration (ORA) IRB Website and within the electronic IRB submissions and reporting system library of forms and templates. As this manual cannot be expected to address every situation or question that might arise, investigators are requested to review IRB guidance materials or contact the IRB Office at (718) 613-8480 to discuss such issues.

**ETHICAL PRINCIPLES IN HUMAN RESEARCH**

DMC is guided by the ethical principles set forth in the Belmont Report created by the National Commission for the Protection of Research Participants of Biomedical and Behavioral research. The three quintessential requirements for the ethical conduct of Human research are:

- **Respect for persons**: Recognition of the personal dignity and autonomy of individuals, and special protection of those persons with diminished autonomy.
- **Beneficence**: Obligation to do no harm and to protect persons from harm by maximizing the anticipated benefits and minimizing possible risks.
- **Justice**: Benefits and burdens of research should be distributed fairly.

The US Federal regulations were established based on the principles of the Belmont Report. When applicable, the principles of the Nuremberg Code and the Declaration of Helsinki may also apply to the research; particularly for transnational research.

All DMC staff must follow the DMC Code of Ethics. In addition, research professionals are expected to following the ethical principles of their scientific and professional disciplines.

**SCOPE**

This policy applies to all DMC workforce and to investigators and key personnel approved to do research by the DMC institutional review board (IRB).
This policy applies to all research conducted by the DMC workforce (regardless of whether or not compensation is received) while on DMC time, utilizing DMC resources (e.g., equipment), or DMC property (including space leased or used by the DMC).

This policy applies to:

- All activities which make DMC engaged in human research,
- All activities for which an IRB determination is made by the DMC IRB, or
- Any activity overseen by the DMC IRB, including research non-compliance and research audits

When the DMC IRB oversees human research carried out by employees from an external site (i.e., is not a legal entity of DMC), the external site must do one of the following:

- If the study is funded by US Department of Health and Human Services (HHS), or any of the federal agencies or departments which are signatories to the Common Rule, either of the following must occur:
  - The external employees can seek IRB approval from their institution, or
  - The external institution may establish an IRB (Reliance) Agreement with the DMC IRB. The external IRB may either designate the DMC IRB on their FWA or any IRB which they rely on the most.

- If the study is NOT federally funded NOR federally supported any of the following options apply:
  - The external employees may seek IRB approval from their institution. 
    *Note: The external employees should consult with their institution’s policy.*
  - The external institution may rely on the DMC IRB; however, either the external site or the DMC IRB may require the establishment of an IRB Reliance (Authorization) Agreement with the DMC IRB.
    *Note: NYC H+H Kings County has established an IRB Reliance Agreement with the DMC IRB.*
  - The DMC IRB can oversee the research; however, the DMC IRB may require the PI to submit documentation (e.g., letter of support) that indicates the external site allows the oversight of the DMC IRB.

**ACRONYMS AND DEFINITIONS**

For a list of acronyms and definitions applicable to this policy and other IRB application materials, please consult the IRB Guidance document called “IRB Acronyms and Definitions,” which is posted in the IRB application and reporting system.

**DETERMINING WHETHER IRB APPROVAL IS REQUIRED**
ACTIVITIES REQUIRING IRB REVIEW AND APPROVAL

An FDA regulated clinical investigation or clinical trial must have IRB approval before the study begins.

In order for a non-FDA regulated activity to be considered research under the HHS regulations, it must be both 1) a systematic investigation and 2) be designed to develop or contribute to generalizable knowledge. In order for research to be considered human research, it must involve *living* individuals *about whom* an investigator conducting research obtains either 1) data through an intervention or interaction with the individual, or 2) individually identifiable private information. All human research must have IRB approval before the study begins.

Some human research activities are exempt from HHS or FDA federal regulations; however, the DMC still has oversight of these activities. **An exemption must be prospectively determined by the IRB.**

The IRB allows for one exception to the prospective determination of exempt research: An independent determination by an investigator is acceptable solely for the purpose of making and documenting representations for reviews preparatory to research using the [Researcher Certification for Reviews Preparatory to Research](#). Preparatory to research activities are automatically considered exempt because identifiers cannot be recorded.

Even when research is exempt from HHS and FDA regulations or when the activity does not meet the definition of human research, the HIPAA/HITECH regulations still apply, if PHI is involved in a research activity. If PHI is involved, a HIPAA waiver, HIPAA Authorization, BAA, DUA, or other HIPAA instrument is usually required.

In general, the activities that require prospective IRB review and approval are:

- Human research (including pilot studies, exempt research, clinical trials, or other clinical investigations, planned emergency research)
- Use of an Humanitarian Use Device (HUD) for a clinical or research purpose (except IRB approval is not needed for certain exceptions for emergency use)
- Research activities that involve an interaction or intervention with a living individual
- Research activities that involve obtaining, accessing, using, reviewing, sharing, or disclosing protected health information (PHI), individually identifiable private data, identifiable sensitive information, or personal data, regardless of whether it is recorded or eventually de-identified.

Activities that require IRB review and approval beyond the initial review include:

- Amendments to previously approved research;
- Continuing review/progress reports;
- Reportable events;
- Closure (final) reports; or
• Other considerations, as described in this policy or regulations.

ACTIVITIES THAT DO NOT REQUIRE IRB REVIEW AND APPROVAL

CLINICAL CARE

Nothing in this policy is intended to limit the authority of a clinician to provide medical care, including to the extent the clinician is permitted to do so under applicable federal, state, local law, or DMC policy.

OFF-LABEL USE OF AN FDA APPROVED DRUG OR BIOLOGIC

If a clinician wishes to use an FDA approved drug/biologic off-label for non-research purposes, the decision to do so is a clinical decision that does not require IRB approval; however, the clinician must comply with any necessary hospital policies including, when applicable, obtaining approval from the Pharmacy.

Off-label use for non-research purposes does not constitute research; therefore, the patient who receives the off-label drug or device may not be treated as a research participant.

For more information, see FDA Information Sheet: “Off-Label” and Investigational Use of Marketed Drugs, Biologics, and Medical Devices.

EMERGENCY USE OF AN INVESTIGATIONAL OR UNLICENSED DRUG, BIOLOGIC, OR DEVICE

Emergency use is the use of a test article (investigational or unlicensed drug, biologic, or device) for a patient 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. Emergency uses are not considered research, but rather the practice of medicine for the treatment of patients with non-FDA-approved products.

If a clinician wishes to prescribe a test article that is considered to be part of a program for expanded access, or for an emergency use, or for compassionate use, the clinician must do the following:

• Contact the Medical Director (or designate) and Department Chair (or designate) to obtain permission before undertaking the emergency use of the unapproved test article and make every reasonable effort to notify the IRB Chair of the test article.
The approvals and notices can be in the form or an e-mail or memo and can be submitted to the IRB using the Application for Reportable Event.

- Comply with all pertinent FDA regulations.
- Contact the manufacturer to make arrangements for delivery of the test article and make sure they are willing to release the test article in accordance with FDA regulations. The supplier of the unapproved test article may require assurance from the DMC that rules and regulations that apply to emergency use are being followed before agreeing to provide the unapproved article.
- If required by the manufacturer, the IRB can release a letter stating there is not sufficient time to obtain IRB approval.
- Contact the FDA to obtain an emergency IND or an emergency IDE, when required, if the manufacturer does not provide one.
- When feasible, prospectively obtain informed consent and assent for the emergency use of an investigational agent. Obtaining informed consent shall be deemed feasible unless, before use of the test article, both the treating physician and another physician who is not otherwise involved in the use of the investigational product certify in writing all of the following, in the patient’s medical record:
  - The patient is confronted by a life-threatening situation necessitating the use of the test article;
  - Informed consent cannot be obtained from the patient because of an inability to communicate with, or obtain legally effective consent from, the patient;
  - Time is not sufficient to obtain consent from the patient’s Legally Authorized Representative; and
  - There is no available alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the patient.
- **Notify the IRB within 5 days after the administration of the test article.** This may be done via e-mail or within the electronic IRB submission and reporting system, using the Application for Reportable Event. The IRB will acknowledge the emergency use.

**TIP:** In general, emergency use of an investigational agent may only be authorized once.

If the future need for use of the test article under similar circumstances is anticipated, an IRB application must be submitted to the IRB for review. In general, the IRB will acknowledge the use of a test article more than once if it is in the best interest of a patient. However, subsequent use without IRB approval may represent serious or continued non-compliance. If considered by the IRB to be serious or continuing non-compliance, the circumstances must be reported to the FDA. For this reason, it is recommended that after one emergency use of an investigational agent the clinician submit an IRB application for use of the test article under similar circumstances.

Emergency use does not constitute research and the patient in whom the drug or device is used under this exception may not be treated as a research participant.
CHANGES NECESSARY TO ELIMINATE APPARENT IMMEDIATE HAZARDS OR TO PROTECT THE LIFE OR PHYSICAL WELL-BEING OF THE RESEARCH PARTICIPANT

Changes in a research activity may be initiated without IRB review and approval when necessary to eliminate apparent immediate hazards or to protect the life or physical well-being of the research participant.

However, these changes must be subsequently reported to the IRB, as outlined in the section on Reportable Events.

IRB APPLICATION SUBMISSION PROCESS

IRB MEETING SCHEDULE

The meeting schedule and deadlines for submitting a full board IRB application are posted on the DMC IRB website.

Note: Exempt and expedited studies are not reviewed by the full board unless an IRB Member defers the review to the full board process.

IRB CONSULTATIONS

In the case of a PI who is submitting a protocol for the first time or an investigator who may not be well-versed in the protocol submission procedures, individualized IRB consultations can be arranged. Specific questions about the IRB policies and procedures, determination of whether a particular protocol is human research or not and what particular forms are required for a particular study can be addressed at any time, in writing or in person, with the IRB administrative staff. Individual appointments with the IRB administrative staff can also be arranged and are strongly recommended for first-time submissions.

TIP: The submission may be shared with an IRB Office Staff or IRB Member for preliminary feedback by sharing the submission in the electronic IRB submission and reporting system for preliminary feedback before it is submitted to the IRB.

ELECTRONIC SUBMISSIONS AND MANAGEMENT OF DMC IRB ACTIVITIES

DMC uses an electronic IRB submission and reporting system for the electronic submissions and management of its IRB activities. Please refer to IRB guidance on electronic IRB submissions and reporting system for more details on how to use the system.
A physician may request approval to use a Humanitarian Use Device (HUD), which is a “medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year.” HUDs cannot be sold for profit except in narrow circumstances and they can only be used in a facility after an IRB has approved their use in that facility, except in emergencies where the physician determines that approval cannot be obtained in time to prevent serious harm or death to the patient (see section on Emergency Use in Policy).

A HUD IRB Application must be completed when submitting an initial request for the IRB approval to use an HUD for clinical purposes. The progress report for the use of a HUD may be reviewed by expedited review at the time of continuing review, unless an IRB Member, or an IRB Chair determines it must go to the full board.

When requesting the use of a HUD for clinical use only, the application does not need to go through the Scientific Review Committee (SRC), nor are COI disclosures required.

The IRB has the authority to set restrictions or limitations when the HUD is used by the clinician.

If a HUD will be used for a clinical investigation (e.g., safety and effectiveness data is collected for a FDA Premarket Approval), a full board IRB application must be completed, in addition to the HUD application, which requires SRC review and applicable COI disclosures.

**CONSIDERATIONS FOR RESEARCH SUBMISSIONS AND IRB REVIEW**

The following considerations are provided for investigators when designing their research project and by IRB Members when reviewing the submission.

**CATEGORIES OF DMC IRB SUBMISSIONS**

There are five types of IRB submissions at DMC:

1. Determination that IRB review is not required
2. Exempt IRB review
3. Expedited IRB review
4. Full (convened board) IRB review
5. Request to use an external IRB

The criteria for each type are described below.
DETERMINATION THAT IRB REVIEW IS NOT REQUIRED

An IRB determination letter may be requested to document activities that do not need IRB approval, provided all the information and supporting documents are provided in the electronic IRB submission and reporting system. Please refer to the “IRB Decision Aid – Application for a Determination Letter to State IRB Approval is Not Required” for guidance.

EXEMPT IRB REVIEW

An exempt determination may be made by the IRB if the proposed study meets the criteria for exempt human research, in accordance with 45 CFR 46.101(b) for non-FDA regulated research or in accordance with 21 CFR 56.104 for FDA regulated research. The exemption categories (1-5) in the IRB application for exempt research apply to non-FDA regulated Human research only. The exemption category 6 applies to both non-FDA Human research and FDA regulated research. Additional FDA exemptions related to the emergency use of a test article are described in the section on Emergency Use.

Federal regulations prohibit applying these exempt categories to research involving prisoners. All research involving prisoners must be expedited or reviewed by the Full Board.

A new study qualifies for exempt review if all of the activities meet the specific criteria of one or more categories outlined as follows:

- **Exemption category 1**: research conducted in established or commonly accepted educational settings, involving normal educational practices, such as
  - Research on regular and special education instructional strategies, or
  - Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

- **Exemption category 2**: research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
  - information obtained is recorded in such a manner that human research participants can be identified, directly or through identifiers linked to the participants; and
  - any disclosure of the human research participants' responses outside the research could reasonably place the participants at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, or reputation.

*Exemption category 2 cannot be applied to research involving children, except for research involving observation of public behavior when the investigators do not participate in the activities being observed.*
• **Exemption category 3**: research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under category 2; if
  o the research participants are elected or appointed public officials or candidates for public office; or
  o federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

• **Exemption category 4**: research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that research participants cannot be identified, directly or through identifiers linked to the research participants.

• **Exemption category 5**: research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:
  o public benefit or service programs;
  o procedures for obtaining benefits or services under those programs;
  o possible changes in or alternatives to those programs or procedures; or
  o possible changes in methods or levels of payment for benefits or services under those programs.

• **Exemption category 6**: Taste and food quality evaluation and consumer acceptance studies,
  o if wholesome foods without additives are consumed or
  o 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.

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**EXPEDITED IRB REVIEW**

A new study may qualify for expedited review if it presents no more than minimal risk to the research participants and it meets other specific criteria, as outlined in the IRB application form. The expedited review categories and applicability to both non-FDA regulated and for FDA regulated research and are fully described within [the Federal Register: November 9, 1998 (Volume 63, Number 216)](https://www.federalregister.gov/documents/1998/11/10/25864/EXPEDITED-IRB-REVIEW).
The standard requirements for informed consent (or its waiver, alteration, or exception) apply to expedited review.

The following types of studies may not be expedited, at the time of initial or continuing review:

- Research involving an IND or IDE.
- A NSR device study.
- Research where the identification of the participants and/or their response would reasonably place them at risk of criminal or civil liability or be damaging to the participants’ financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections are implemented so that the risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
- Classified research.

Although a study may qualify to be reviewed by expedited review during continuing review or an amendment, a study may not be expedited at the time of initial review if the research includes any of the following:

- Biomedical interventions with children, pregnant women, neonates, prisoners, or cognitively impaired adults
- Certificate of Confidentiality

Even when a study qualifies for expedited review, the IRB may defer the initial review to the convened (full) board (for sensitive issues, study design concerns, etc.). In this situation, the study may continue to be reviewed by expedited review procedures for any follow-up required by the convened IRB or for the review that is carried out at the time of continuing review, unless the IRB otherwise determines the review must be carried out by the convened board.

The following expedited review categories are used for initial and continuing review:

- **Expedited research review category #1A:** research on drugs for which an investigational new drug application (21 CFR Part 312) is not required.

- **Expedited research review category #1B:** research on medical devices for which
  - an investigational device exemption application (21 CFR Part 812) is not required; or
  - the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

- **Expedited research review category #2A:** Collection of blood samples by finger-stick, heel-stick, ear-stick, or venipuncture from healthy, non-pregnant adults who weigh at least 110 pounds.
For these research 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.

- **Expedited research review category #2B:** Collection of blood samples by finger-stick, heel-stick, ear-stick, or venipuncture from adults and children, considering the age, weight, and health of the research participants, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected.

  *For these research 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.*

This category may include non-healthy adults, pregnant adults, and adults who weigh less than 110 lbs., if requested in the IRB application materials.

- **Expedited research review category #3:** Prospective collection of biological specimens for research purposes by noninvasive means, not limited to the following examples, which are generally considered noninvasive:
  - Hair and nail clippings in a non-disfiguring manner;
  - Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
  - Permanent teeth if routine patient care indicates a need for extraction;
  - Excreta and external secretions (including sweat);
  - Un-cannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;
  - Placenta removed at delivery;
  - Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
  - 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;
  - Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
  - Sputum collected after saline mist nebulization;

- **Expedited research review 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.*
• **Expedited research review 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:* As permitted by OHRP, this category includes research involving materials that were previously collected for either non-research or research purposes, provided that any materials collected for research were not collected for the currently proposed research. Research may involve materials that will be collected solely for non-research purposes.

• **Expedited research review category #6:** Collection of data from voice, video, digital, or image recordings made for research purposes.

• **Expedited research review 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.

The following expedited review categories are used for continuing review of previously approved research:

• **Expedited research review category #8A:** research that is permanently closed to the enrollment of new research participants; when all of the research participants have completed all research-related interventions; and the research remains active only for long-term follow-up of research participants.

• **Expedited research review category #8B:** research where no research participants have been enrolled and no additional risks have been identified.

• **Expedited research review category #8C:** research where the remaining research activities are limited to data analysis.

• **Expedited research review category #9:** Continuing review of research, that is not conducted under an investigational new drug application (IND) or investigational device exemption (IDE) 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.

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**FULL (CONVENED) IRB REVIEW**

Any study that does not meet the criteria for exempt or expedited review must be reviewed by the full board.
REQUEST TO USE AN EXTERNAL IRB FOR MULTI-SITE RESEARCH PROJECTS

An external IRB is any IRB other than the DMC IRB that reviews and approves a multi-site research project that includes DMC. This can be a Central IRB, a Commercial IRB, a Main Study Site IRB, or a Single IRB; however, the DMC IRB may be required to establish an IRB Authorization (Reliance) Agreement with the external IRB. The DMC IRB must acknowledge external IRB approval, and confirm DMC requirements are met, before the research may begin at DMC.

Any external IRB that oversees DMC research must enter into an IRB Reliance (Authorization) Agreement with SUNY DMC for all federally funded research and may be required to establish such an agreement for non-federally funded research. At the time of this writing, the SUNY DMC has entered into IRB Reliance (Authorization) Agreement with the following IRBs:

- National Cancer Center Central IRB (1, 2, 3, & 4)
- Biomedical Research Alliance of New York (BRANY) IRB

Unless the DMC IRB defers review to an external IRB, an external IRB CANNOT be used for any research involving any of the following:

- Investigational device studies involving an IDE (external IRB prohibited by FDA);
- DMC as a single research site; or
- Research that has been reviewed by the DMC IRB and determined to require revisions or has not been approved by the DMC IRB.

When using an external IRB, the research team must follow the procedures, policies, directives, and practices of the external IRB, the DMC, the IRB Authorization (Reliance) Agreement, and the sponsor.

The PI and research staff must comply with the determinations and requirements of the both the external IRB and the DMC IRB. DMC is responsible for ensuring compliance with the IRB’s requirements at the DMC.

Each institution involved in the multi-site project is responsible for ensuring compliance at their site. Research staff from external sites must consult their own institutional policies to determine if other requirements apply. Where necessary the specific affiliate institutional approvals (e.g., STAR approval at NYC H+H Kings County) may be required before a study may be started.

All reportable events must be reported to the external IRB.

PROCEDURES FOR REQUESTING AN EXTERNAL IRB REVIEW AND APPROVAL

**IMPORTANT:** When requesting the review and approval of human research by an external IRB,
the PI must complete the required external IRB Application (according to the guidance and directions of the external IRB) and the DMC IRB’s “Application for External IRB Oversight.”

**CAUTION:** The DMC often collaborates with employees from NYC H+H Kings County. If employees from NYC H+H Kings County are included as investigators on a **federally funded** study, please use the **BRANY IRB** or collaborate with NYC H+H Kings County to establish an IRB Reliance (Authorization) Agreement with the External IRB and NYC H+H Kings County.

**TIP:** While waiting for approval of the external IRB application, one may wish to begin the submission to the DMC IRB to ensure all local requirements will be met when submitting the DMC IRB’s “Request to Use an External IRB Application.” In particular, please ensure the following are completed on a timely basis:

1. Ancillary reviews, if applicable
2. Training
3. Conflict of Interest (COI) disclosures

The IRB Office will forward the IRB Reliance Agreement to the IO for signature. The DMC IRB will acknowledge the approval of the external IRB’s approval once it has certified that all local research context requirements are met, including all local training and conflict of interest requirements. In general, the DMC IRB will not require changes to the model consent approved by the external IRB; however, the DMC IRB may require an addendum to the consent, which would also need to be approved by the external IRB.

The external IRB must approve the research and the DMC IRB must acknowledge the external IRB approval before any research activities at the DMC site may begin. The DMC IRB has prepared a guidance document which summarizes local research context issues, which may be provided to the external IRB.

The expiration date of IRB approval will be determined by the external IRB.

All required ancillary reviews must take place before the research may begin. If required by the External IRB, the DMC IRB can issue a preliminary letter stating local ancillary reviews are complete.

If the DMC IRB receives a notice of approval of continuing review, yet not all of the investigators have updated their local training or conflict of interest requirements, the delinquent investigators cannot participate in the research, until all of the requirements are met of the delinquent investigators.

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**DMC ACKNOWLEDGEMENT PROCESS AFTER EXTERNAL IRB APPROVAL**

Before acknowledging the external IRB approval, the DMC will confirm:
• An IRB Reliance Agreement, when required, has been fully executed between DMC (including Kings County Hospital Center, if applicable) and the external IRB
• All required ancillary reviews are complete
• All required training is complete
• All required conflict of interest disclosures are complete and approved

ADDITIONAL PROTECTIONS REQUIRED BY THE DMC IRB WHEN USING AN EXTERNAL IRB

In general, an External IRB serves as a Privacy Board to approve HIPAA authorizations or HIPAA waivers, under the HIPAA regulations. If an External IRB does not serve as a Privacy Board, such as the NCI CIRB, it does not have the authority to approve HIPAA authorizations or HIPAA waivers. When an external IRB does not have the authority to approve any HIPAA documents, the DMC IRB (which does serve as a Privacy Board) must approve any HIPAA documents.

If boiler plate language or addendum documents are required to be added to the informed consent or information sheet documents by the DMC IRB, the external IRB must also approve of the additional requirements.

When there is a prospect of direct therapeutic benefit to potential research participants, the PI is expected to develop a plan to enroll participants with limited English proficiency (LEP), to be approved by the external IRB and acknowledged by the DMC IRB. If the DMC PI wishes to use the certified DMC short forms, the external IRB must approve the use of these documents. The external IRB may direct whether the informed consent form and/or a summary of what is to be said to a potential research participant must be translated and the circumstances when these are to be used.

DMC reserves the right to place enrollment on hold, suspend or terminate the research activity or request additional protections at the DMC site at any time. At such time, the DMC IRB or Institutional Official will promptly notify the external IRB of these actions; however, the PI may also be required to notify the external IRB, within the external IRB’s specified reporting deadlines. Amendments requested by the DMC IRB must be submitted to the external IRB, within the time frame requested by the DMC IRB. The PI must provide the results of the request to the DMC IRB within 5 days if the external IRB issues a disapproval or otherwise within 30 days.

Although a study is under the primary jurisdiction of the external IRB, the following is required by the DMC IRB:
• All IRB notices or letters from the external IRB must be submitted to the DMC IRB for local acknowledgement, within 30 days of notice, by the External IRB.
• Whenever there are changes to materials that require an IRB stamp prior to use and the external IRB does not provide a stamp, a DMC IRB amendment must be submitted to the DMC IRB to request that the materials be stamped.
• Whenever there are changes to the local study site personnel, an IRB amendment must be submitted to the DMC IRB. When adding research staff, please indicate whether the new research staff are considered investigators for the purposes of COI as defined by the DMC COI policy. New study site personnel may not participate in the research until the DMC IRB acknowledges the addition of study staff.
• The DMC study team must complete a continuing review (progress) report for the DMC IRB to verify that all local COI, training, or additional local research context requirements are up to date at the time of continuing review.
• Post approval monitoring may be conducted by either the External IRB or the DMC IRB, as indicated or required.

In addition to the reporting requirements of the external IRB, the following events must be immediately reported to the DMC IRB:
• Any privacy breach that occurs at DMC must be immediately reported to the DMC IRB and the DMC Privacy Officer.
• Any information security breach that occurs at DMC must be immediately reported to the DMC IRB and the DMC Data Security Officer.
• Any event involving the death of a research participant from the DMC site, when the death is related, probably related, or possibly related to participation in the research.
• Whenever it is discovered that a research participant from the DMC site has been incarcerated, if any research interventions must take place while under incarceration.
• Any event that occurs at DMC that requires mandated reporting to a State or Federal Department or Agency, including:
  o Suspension or termination of IRB approval of research
  o Unanticipated problems involving risks to research participants or others
  o Serious or continuing non-compliance

INVESTIGATOR QUALIFICATIONS

The IRB needs information about the qualifications of the investigator(s) to conduct and supervise the proposed research. Depending upon the nature and risks of the proposed research and the relationship between the IRB and the investigator or the institution where the proposed research is being conducted, this may be relatively simple and straightforward or it may entail a more involved assessment. If the IRB has no knowledge of the investigator the IRB will likely need to take additional steps to evaluate the investigator’s qualifications.

Such steps may include, as appropriate, reviewing the CV of the PI or other research staff, verifying professional associations and medical licensure, or reviewing relevant publications and the investigator's training in good clinical practice, as appropriate. The IRB and SRC may also need to assess the investigator’s training and experience specifically related to the proposed study, particularly if the proposed research involves extremely high risks, vulnerable research participants, or novel technologies.

If a PI is external to DMC, (s)he may need to submit a copy of his or her CV with the IRB application, to assist the IRB in the evaluation of the PI qualifications, particularly if the IRB is not familiar with the PI’s research.

For clinical trials overseen by a PI from an external site, other than NYC H+H Kings County, the PI should provide a statement from an administrator of the external institution to confirm the PI qualifications. This should come from a Credentialing Office, IO, Department Chair, or Dean
and include information about the clinical investigator’s qualifications, his or her credentials and licensure, and whether there have been any institutional disciplinary actions brought against the PI.

If a PI does not have the appropriate privileges or credentials to carry out a research intervention in a research study, the applicable activities may be conducted by another appropriately qualified PI (multiple PIs are permitted), or Co-investigator, approved by the IRB.

The IRB may check lists posted on FDA’s website, Clinical Investigator Status (Biologics), Inspection Classification Database Search, Clinical Investigators - Disqualification Proceedings, Inspections, Compliance, Enforcement, and Criminal Investigations to determine whether an investigator has been the subject of an inspection by the agency and the results of such inspections (e.g., Warning). The FDA also posts on its website a listing of all investigators who have been notified of the initiation of a disqualification proceeding or have been disqualified. The IRB may check FDA’s Inspections, Compliance, Enforcement, and Criminal Investigations website for information related to clinical investigator inspections, warning letters, disqualification proceedings, and debarments.

INVESTIGATORS AND RESEARCH TEAM

PRINCIPAL INVESTIGATOR

The principal investigator (PI) oversees scientific, technical, and day-to-day management of the research. The PI must have appropriate qualifications and experience. The PI holds the lead responsibility for the research protocol, including oversight of its implementation and the activities of other investigators and research staff, and management of any funding associated with the protocol; the PI is held accountable for all compliance.

Protocols that require skills beyond those held by the PI must be modified to meet his or her skills, or the PI must include on the protocol one or more additional qualified co-investigator(s).

PIs are expected to be on-site where the research takes place at least 50% of their time or require one or more additional qualified co-investigator(s) to be available and delegated within the IRB application materials to address any safety and leadership concerns.

PI STATUS

For the purposes of this policy, the PI listed on an IRB application must be a seasoned investigator with a field-specific terminal degree who is a Faculty Member at DMC or who otherwise meets at least one of the following eligibility criteria:
• Have clinical privileges at NYC H+H Kings County
• Qualify to be a PI at an external site (other than NYC H+H Kings County), which includes an activity which makes DMC engaged in human research (see OHRP guidance: Engagement of Institutions in Human Subjects Research (2008)), including when federal funding or support is provided to DMC or when the research includes one of the following co-investigators or key personnel:
  o Employee of SUNY DMC
  o Employee of the Research Foundation for SUNY-Downstate Medical Center
  o Resident or Fellow trained under a GME program affiliated with DMC
  o Student in a DMC Academic Program
• Be a faculty member under recruitment to DMC approved to be a PI by a written memo or an e-mail from a Dean
• Be approved to be a PI by a written memo or an e-mail from the DMC Institutional Official

A PI who is an external employee to DMC and listed on a DMC IRB application agrees to abide by DMC policies for the duration of the study.

MULTIPLE PRINCIPAL INVESTIGATORS

In general, only one individual may serve as a PI for each IRB application; however, for the purposes of this policy, multiple principal investigators are permitted on an IRB application when multidisciplinary efforts require more than one PI to be responsible for the scientific and technical direction of the project.

A rationale for choosing a multiple PI approach should be described in the IRB application materials and include a description of the roles, the responsibilities, and the working relationship of the identified PIs. Each PI must have the necessary qualifications for their role and must contribute towards the proposed goals of the research.

The first PI listed in the IRB application must be affiliated with the institution that is submitting the application and will serve as the contact PI.

Each PI must electronically sign the initial submission or the amendment submission when an additional PI is added, in the electronic IRB submission and reporting system. At least one PI must electronically sign all other submissions to the IRB.

PI RESPONSIBILITIES

The PI must uphold professional and ethical standards and practices when conducting research. The responsibilities of investigators are defined in this policy, the IRB application, and the
Additional responsibilities may be defined by a sponsor or other applicable agreements. As applicable to the research, the PI responsibilities include, but are not limited to, the following obligations to

- Conduct ethical research and protect the rights and welfare of research participants;
- Develop a research plan that is scientifically sound and minimizes risk to the research participants;
- Comply with all Federal and State laws and regulations, contractual obligations, and DMC policies;
- Ensure that risks to research participants are minimized:
  - by using procedures which are consistent with sound research design and which do not unnecessarily expose research participants to risk, and
  - whenever appropriate, by using procedures already being performed on the research participants for diagnostic or treatment purposes;
- Ensure that all research involving participants receives IRB review and approval in writing before commencement of the research;
- Comply with all IRB decisions, conditions, and requirements;
- Recruit research participants in a fair and equitable manner;
- Obtain and document informed consent as required by the IRB and ensure that no research participant is involved in the research prior to obtaining their consent, unless waived;
- Have plans to monitor the data collected for the safety of research participants;
- Protect the privacy of research participants and maintain the confidentiality of data;
- When some or all of the research participants are likely to be vulnerable to coercion or undue influence, include additional safeguards in the study to protect the rights and welfare of these research participants;
- Have a procedure to receive complaints or requests for additional information from research participants and respond appropriately;
- Submit accurate IRB application materials and conduct research according to all written approvals and applicable contractual obligations;
- Provide timely progress reports and associated materials for continuing review;
- Request amendments on a timely basis and in accordance to IRB procedures;
- Promptly obtain IRB review and approval of proposed changes before implementing a change, except when necessary to eliminate apparent immediate hazards or to protect the life or physical well-being of the research participant;
- Promptly review all IRB approved materials and request any administrative corrections (e.g., errors in IRB letters, stamps, approved documents, etc.), if needed;
- Promptly report all required events or incidents to the IRB within the required deadlines;
- Ensure protocols receive timely continuing IRB review and approval;
- Ensure proper study closure;
- Oversee and ensure qualified research staff;
- Ensure all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions;
• Ensure availability of medical or psychological resources that research participants might require as a consequence of the research;
• Assure all procedures in a study are performed with the appropriate level of supervision;
• When procedures require an investigator to have a specific license, be credentialed, or be otherwise qualified, ensure only appropriate individuals perform such procedures under applicable laws or DMC policies;
• Assure that all key personnel are educated in the regulatory requirements regarding the conduct of research and the ethical principles upon which they are based;
• As applicable to the study, prospectively obtain and document voluntary consent, parental permission, pediatric assent, and HIPAA research authorization using the IRB–approved, stamped form(s);
• Securely maintain complete research records, in accordance with regulatory time frames and DMC policies;
• Cooperate with any audit, sponsor site visit, or government investigation;
• Disclose conflicts of interest on a timely basis;
• Ensure appropriate use and review of laboratory reports;
• Follow correct billing practices, policies, and CMS regulations for research activities, including those for qualifying/deemed clinical trials;
• Follow policies for students and volunteers;
• Obtain appropriate approvals of the research budget and contracts related to the research;
• Ensure adequate resources necessary to protect research participants, including:
  o Access to a population that would allow recruitment of the required number of research participants
  o Sufficient time to conduct and complete the research
  o Adequate numbers of qualified staff
  o Adequate facilities
• Supervise the administration of drugs, biologics, and devices, and ensure prescriptions (or medication orders) for study drugs and biologics are authorized;
• Ensure all Applicable Clinical Trials are registered on www.clinicaltrials.gov and updates are maintained based on the required frequency
• Ensure the required language is provided in the consent document for Applicable Clinical Trials;
• Obtain a Certificate of Confidentiality, when applicable;
• Ensure multi-site studies have IRB approval;
• Notify the IRB of any relocation of research activities;
• Notify the IRB and Department Chair of any planned departures or an extended leave of absence
• Ensure a Materials Transfer Agreement (MTA) is established, when required, and in consistency with IRB approved materials;
• Maintain an enrollment master list of research participants that were enrolled into a research study, unless waived by the IRB;
• Maintain a current list of study staff, CVs/Resumes, credentials, and their respective training certifications;
• Follow FDA regulations when conducting a clinical trial or device study;
• For FDA regulated clinical trials, complete the proper FDA forms and submit them to both the sponsor and the IRB, such as FDA Form 1571 (IND Application) and FDA Form 1572 (Statement of Investigator), for new submissions and when amended; and
• Electronically sign his/her IRB application in the electronic IRB submission and reporting system
• Ensure that the Scientific Review Committee (SRC) and Department Chair and other required ancillary reviewers electronically sign his/her IRB application in the electronic IRB submission and reporting system or provide an alternate form of signature approval (e.g., signed letter, memo, application, etc).

CO-INVESTIGATORS AND KEY PERSONNEL

Co-investigators and key personnel assist the PI in fulfilling his/her responsibilities as outlined in the PI Responsibilities section of this document. For the purposes of this policy an investigator or key personnel is any individual who is involved in conducting human research studies, whose involvement would include:
• obtaining information about living individuals by intervening or interacting with them for research purposes;
• obtaining identifiable private information about living individuals for research purposes;
• obtaining the voluntary informed consent of individuals to be research participants in research; and
• studying, interpreting, or analyzing identifiable private information or data for research purposes.

Hospital staff, research coordinators and research assistants must be listed as a co-investigator or key personnel if they will conduct human research including any of the activities described above; however, the FDA provides an exception for delegating clinical trial tasks to hospital staff and residents, as described in the section below.

Co-investigators and key personnel can include physicians, scientists, nurses, administrative staff, teachers, and students, among others. Some research studies are conducted by more than one investigator, with one investigator designated as the PI with overall responsibilities for the study.

Co-investigators and key personnel are responsible for research protocols with research participants, and must have suitable qualifications, including: (1) familiarity with research methods and procedures; (2) familiarity with research regulations and other applicable regulatory requirements; and (3) certificates for required training courses.

The PI may wish to distinguish between co-investigators and key personnel on the IRB application, as it may be a preference of a sponsor or a publication; however, for the purpose of
this policy, they are treated the same, even if they are distinguished separately on the IRB application or related materials.

**DELEGATION OF CLINICAL TRIAL TASKS TO HOSPITAL STAFF AND RESIDENTS**

For FDA regulated clinical trials (IND, IDE, NSR device studies), the PI may delegate certain responsibilities; however, the PI must provide adequate supervision of those who tasks are delegated. For more information on investigator responsibilities, see [FDA Guidance for Investigator Responsibilities](https://www.fda.gov/regulatory-information/search-fda-guidance-documents) and the [FDA FAQs for Form 1572](https://www.fda.gov/regulatory-information/search-fda-guidance-documents).

Hospital staff, including nurses, residents, fellows or office staff who provide ancillary or intermittent care but who do not make a direct and significant contribution to the clinical data do not need to be listed as an investigator or key personnel on the IRB application for FDA regulated clinical trials, when they have only an occasional role in the conduct of the research (e.g., an on-call physician who temporarily dealt with a possible adverse effect or a temporary substitute for any research staff). The PI must ensure that any individual to whom a task is delegated is appropriately qualified, by education, training, experience, licensure, certification, or credentialing, to perform the delegated task. The IRB strongly encourages the PI to maintain a delegation log in the research record to describe the delegated tasks, qualifications, and training, to avoid any appearance of non-compliance. In all cases, a qualified clinician is responsible for all trial-related medical decisions and care.

Concerning residents on rotation or temporary nursing staff, it may be difficult to prospectively identify those individuals who might perform specified protocol procedures or collect clinical data. Specific names of the rotational staff do not have to be listed in the IRB application. Instead, to successfully address this scenario, the names of such individuals and the procedures they are expected to perform should be documented in the research records.

The decision about whether to list other hospital staff (e.g., pharmacist, nurse, medical technologist, x-ray technician, sonographer, research coordinator, statistician, etc.) as a co-investigator or key personnel on the IRB application is a matter of judgment, dependent upon the contribution that the individual makes to the study. For example, a pharmacist may prepare test articles and maintain drug accountability for many clinical studies that are ongoing concurrently at an institution. Because the pharmacist would not be making a direct and significant contribution to the data for a particular study, it would not be necessary to list the pharmacist as a co-investigator in the IRB application; however, (s)he should be listed in the investigator’s study records and may be listed as non-research staff on the IRB application.

Generally, a research coordinator has a greater role in performing critical study functions and making direct and significant contributions to the data. For example, if a research coordinator is recruiting research participants, collecting or evaluating study data, and maintaining study records, (s)he may be listed as a co-investigator or key personnel. Some PIs prefer to list research coordinators as research staff if they have an intellectual role on the study or when they can defend the results of the study.

Delegated staff members are encouraged to take CITI training, but are not required to do so.
NON-RESEARCH STAFF

In general, individuals that carry out activities to support a research study who are doing something that would not make them an investigator, do not need to be considered an investigator on an IRB application, and therefore would not need to complete the requirements (e.g., training and COI disclosures) of an investigator. These individuals can be listed as non-research staff, if desired.

Non-research staff may perform routine clinical or administrative services to support research (e.g., perform a clinical lab test, take an x-ray, perform healthcare operations activities, etc.) provided these are part of their routine responsibilities without being listed as an investigator; however, they cannot collaborate as an investigator or conduct any research activities.

Some examples of non-research activities, may include, but are not limited to the following:

- performing a commercial or other service (e.g., qualified laboratory services, transcription services, obtaining blood or urine, radiology services, nursing services) for investigators, provided all of the following conditions are met:
  - the services performed do not merit professional recognition or publication privileges;
  - the services performed are typically performed by those institutions for non-research purposes; and
  - the individual does not administer any study intervention being tested or evaluated under the protocol, or
- releasing identifiable information, materials, or specimens to investigators,
- reviewing identifiable information for the purposes of auditing or other healthcare operations activities,
- receiving de-identified specimens for the purposes of analytical testing,
- reviewing de-identified data for the purpose of authoring, describing, or presenting a research study.

Individuals performing healthcare operations activities relevant to the research (e.g., research audit, audit preparation, IRB review, and protocol development) including IRB members or consultants who advise and guide the research staff members are not considered research staff, if their primary purpose is to fulfill a healthcare operations activity.

Non-Research staff members are encouraged to take CITI training, but are not required to do so.

KEY CONTACT OR IRB LIAISON

Key contacts and IRB liaisons may be listed on the IRB application and registration form to have access to the IRB application materials, or a member of the study team can share access in the electronic IRB submission and reporting system. They may review these materials as a
Healthcare Operations Activity. Examples of key contacts include administrative personnel that have a need to follow or assist in the research, but not conduct investigator activities.

External sites with an IRB Authorization Agreement may have a liaison who receives copies of communications from the IRB. These individuals are not required to be listed as key contacts in the IRB application, but may have access to the study files.

ADEQUACY OF RESEARCH SITE

When the IRB is not familiar with the research site, the IRB may require additional assessment of the site’s adequacy. The IRB may need to assess the adequacy of the facility’s staff and medical equipment, including the adequacy of emergency or specialized care, if the need arises. If needed, the IRB may require a statement from the research site indicating the site is adequate or require a description from the PI that includes a description of the facility where the research will take place, including staffing and resources relevant to the research under review.

GENERAL CRITERIA FOR IRB APPROVAL

The IRB must determine all of the criteria for IRB approval are satisfied, before final approval is granted. The IRB members must refer to the criteria specified in Federal Regulations as outlined in this policy. This is carried out during the review process. If any of the criteria are not met, revisions must be requested.

EXEMPT RESEARCH

In order to approve exempt human research, the IRB must determine that the research as described in the IRB application and associated materials meets the specific criteria for exempt research. The IRB does not allow an investigator or others with a conflict of interest to make an exempt determination.

The SRC and Department Chair must approve exempt research prior to submission to the IRB, by electronically signing the submission before the IRB can approve the research.

The HIPAA regulations apply to exempt research involving PHI and, therefore, the IRB will confirm the appropriate and relevant protections are in place (e.g., HIPAA authorization, HIPAA waiver, DUA, BAA, etc.) for such research.

The IRB will confirm the research meets all requirements and verify it meets the criteria for exempt research; however, it may require additional protections, particularly when vulnerable populations are involved.
NON-EXEMPT HUMAN RESEARCH

In order to approve non-exempt human research or a clinical investigation, the IRB must determine all of the following requirements (as described in 45 CFR 46.111 and 21 CFR 56.111) are satisfied, based on review of IRB application materials:

- Risks to research participants are minimized:
  - by using procedures which are consistent with sound research design and which do not unnecessarily expose research participants to risk, and
  - whenever appropriate, by using procedures already being performed for diagnostic or treatment purposes.

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

- Selection of research participants is equitable. In making this assessment the IRB takes into account the purposes of the research, the adequacy of inclusion and exclusion criteria, and the setting in which the research will be conducted. The IRB is particularly cognizant of the special problems of research involving interactions or interventions with vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

- Informed consent and HIPAA research authorization will be sought from each prospective research participant or their LAR, in accordance with, and to the extent required by the federal regulations and will be appropriately documented, unless waived.
  - The IRB members review the informed consent document to ensure all required elements and appropriate additional elements are provided to the research participant at the time of initial review.
  - At the time of continuing review, the IRB must also review the informed consent document to determine if any additional changes are required.

- When appropriate, the research plan must make adequate provision for monitoring the data collected to ensure the safety of research participants.

- When appropriate, there are adequate provisions to protect the privacy of research participants and to maintain the confidentiality of data.

- When some or all of the research participants 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, the IRB must evaluate whether additional safeguards have been included in the study to protect the rights and welfare of these research participants based on the IRB application materials. The IRB may require additional safeguards, if needed.
• In order to approve research involving some or all research participants that include vulnerable populations, the IRB must also ensure the research is in compliance with regulations to the extent required by 45 CFR 46, subpart B, C, and D and 21 CFR 50, subpart D and DMC Policies. See next sections for more details.
• FDA requires the sponsor or the sponsor-investigator to determine whether an IND or IDE is required for a particular study. The IRB may request the basis for the determination or request supporting documentation from the FDA. If the IRB is unable to resolve the issue, it will be considered a controverted issue and cannot approve the study until the matter is resolved.
• For investigational device studies, the IRB’s determination that a device study is significant risk (SR) or non-significant risk (NSR) can be made at a convened meeting. A SR device study must have an IDE from the FDA before the IRB can approve the investigation.

RESEARCH INVOLVING VULNERABLE POPULATIONS

CHILDREN

45 CFR Subpart D and 21 CFR 50 Subpart D (for FDA regulated research) applies to all research involving children (including neonates).

The IRB must make the determinations necessary to approve the research found in the section of the regulations. The IRB Members may document their determinations in the electronic IRB submission and reporting system.

When applicable, assent and parental permission must be prospectively sought and documented. In general, assent of children over the age of seven (7) is expected, unless the IRB waives the requirement for such.

Research on children must be reviewed and categorized into one of the following allowable categories, provided the criteria listed below each category are also met:

• **Category 404:** Human research or a clinical investigation not involving greater than minimal risk (45 CFR 46.404 and 21 CFR 50.51)
  - Requires assent of the child (unless waived); and
  - The IRB may find that permission of one parent (or legal guardian) is sufficient.

• **Category 405:** Human research or a clinical investigation involving greater than minimal risk but presenting the prospect of direct benefit to the individual research participants (45 CFR 46.405 and 21 CFR 50.52)
  - Requires assent of the child, unless waived;
  - The IRB may find that permission of one parent (or legal guardian) is sufficient (unless waived);
o The IRB must find that the intervention or procedure holds out the prospect of direct benefit for the individual participant, or by a monitoring procedure that is likely to contribute to the participants' well-being;
o The risk is justified by the anticipated benefit to the participants; and
o The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.

**Category 406:** Human research or a clinical investigation involving greater than minimal risk (minor increase over minimal risk) but no prospect of direct benefit to the individual research participants but likely to yield generalizable knowledge about the research participants' disorder or condition. (45 CFR 46.406 and 21 CFR 50.53)
o Requires assent of the child, unless waived;
o The permission, unless waived, must be obtained by both parents (or legal guardians), unless one is deceased, unknown, incompetent or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child;
o The risk represents a minor increase over minimal risk;
o The intervention or procedure presents experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
o The intervention or procedure is likely to yield generalizable knowledge about the participants' disorder or condition which is of vital importance for the understanding or amelioration of the participants' disorder or condition; and
o If children who are wards of the state or any other agency, institution, or entity are included, additional requirements of 45 CFR 46.409 must also be met.

**Category 407:** Human research or a clinical investigation that is not otherwise in category 404, 405, or 406, which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. (45 CFR 46.406 and 21 CFR 50.54)
o Requires assent of the child (unless waived)
o The permission (unless waived) must be obtained by both parents (or legal guardians), unless one is deceased, unknown, incompetent or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child;
o The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
o If children who are wards of the state or any other agency, institution, or entity are included, additional requirements outlined in 45 CFR 46.409 must be met; and
o The OHRP (or by the FDA, if FDA regulated) must also approve the research.

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**CHILDREN WHO ARE WARDS**

In addition to the requirements outlined above, any research involving a child who is a ward (i.e. in custody or oversight by any state or city agency) must be described in the IRB application.
Additional applicable protections must be provided for the Wards as described in 45 CFR 46.409 and 21 CFR 50.56.

**PREGNANT WOMEN, FETUSES, NEONATES, IN-VITRO FERTILIZATION**

When reviewing research involving pregnant women, fetuses, and neonates the IRB must ensure it satisfies all of the conditions covered by [Subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates](https://www.hhs.gov/). 

**PREGNANT WOMEN OR FETUSES**

Pregnant women or fetuses may be involved in research if all of the following conditions are met:

- Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
- The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
- Any risk is the least possible for achieving the objectives of the research;
- If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions;
- If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
- Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- For children who are pregnant, assent and parental/legal guardian permission are obtained in accord with the provisions of the IRB;
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
• Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
• Individuals engaged in the research will have no part in determining the viability of a neonate.

NEONATES OF UNCERTAIN VIABILITY AND NONVIALE NEONATES
Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

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

NEONATES OF UNCERTAIN VIABILITY.

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

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

NONVIALE NEONATES

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

• Vital functions of the neonate will not be artificially maintained;
• The research will not terminate the heartbeat or respiration of the neonate;
• There will be no added risk to the neonate resulting from the research;
• The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
• The legally effective informed consent of both parents of the neonate is obtained. Waivers and alteration provisions do not apply; however, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest.

VIABLE NEONATES
A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements for Children.

RESEARCH INVOLVING PLACENTA, DEAD FETUS, OR FETAL MATERIAL

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

NOTE: At the time of this writing, the Downstate Office of General Counsel determined there are no additional regulatory requirements for the state of NY.

If information associated with material described in this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research participants and all IRB requirements applicable.

RESEARCH NOT OTHERWISE APPROVABLE WHICH PRESENTS AN OPPORTUNITY TO UNDERSTAND, PREVENT, OR ALLEVIATE A SERIOUS PROBLEM AFFECTING THE HEALTH OR WELFARE OF PREGNANT WOMEN, FETUSES, OR NEONATES.

DMC may conduct research that the IRB does not believe meets the requirements for pregnant women, fetuses, or neonates, only if:

• The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and
• OHRP, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined either:
  o That the research in fact satisfies the conditions for research with pregnant women or fetuses, as applicable; or
  o The following:
✓ The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;
✓ The research will be conducted in accordance with sound ethical principles; and
✓ Informed consent will be obtained in accordance with the informed consent provisions

PRISONERS

When reviewing research involving prisoners the IRB must ensure it satisfies all of the conditions covered by Subpart C - Additional Protections Pertaining to Biomedical and Behavioral research Involving Prisoners as Subjects.

The IRB Member who is the prisoner representative must review the research. If the study is federally funded or supported, the OHRP must also approve the research. Prisoner research may not be reviewed under exempt review procedures. In order to approve research involving prisoners, the IRB must find that the proposed research falls into one of the permissible categories of research, and make the following seven findings:

1. The research under review represents one of the permissible categories of research:
   - **Category #1:** Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the research participants;
   - **Category #2:** Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the research participants;
   - **Category #3:** Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after OHRP has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his/her intent to approve such research; or
   - **Category #4:** research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the research participants. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after OHRP has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research.

2. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his
or her ability to weigh the risks of the research against the value of receiving such advantages in the limited-choice prison environment is impaired;

3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;

4. Procedures for the selection of research participants within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the PI provides the IRB with written justification for following some other procedures, control research participants must be selected randomly from the group of available prisoners that meet the characteristics needed for that particular research proposal;

5. The information is presented in language that is understandable to the subject population;

6. Adequate assurance exists that parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and

7. Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences, and for informing participants of this fact.

In order to make these findings, the IRB must be familiar with the specific conditions in the local prison(s) or jail site(s) that are pertinent to protections, before approving the proposal for the local site.

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**EPIDEMIOLOGIC RESEARCH INVOLVING PRISONERS**

Health and Human Services has waived the applicability of 45 CFR 46.305(a)(l) and 46.306(a)(2) for certain research conducted or supported by HHS that involves epidemiological studies that meet the following criteria:

1. In which the sole purposes are:
   a. To describe the prevalence or incidence of a disease by identifying all cases, or
   b. To study potential risk factor associations for a disease, and

2. Where the IRB has approved the research and has fulfilled its duties under 45 CFR 46.305(a)(2)–(7) and determined and documented that the following conditions are met:
   a. The research presents no more than minimal risk and no more than inconvenience to the research participants, and
   b. Prisoners are not a particular focus of the research.

3. The specific type of epidemiological research subject to the waiver involves no more than minimal risk and no more than inconvenience to the research participants. The waiver would allow the conduct of minimal risk research that does not now fall within the categories set out in 45 CFR 46.306(a)(2).

4. The range of studies to which the waiver would apply includes epidemiological research related to chronic diseases, injuries, and environmental health. This type of research uses epidemiologic methods (such as interviews and collection of biologic
specimens) that generally entail no more than minimal risk to the research participants.

5. In order for a study to be approved under this waiver, the IRB would need to ensure that, among other things, there are adequate provisions to protect the privacy of research participants and to maintain the confidentiality of the data.

**NEWBORN SCREENING SPOTS**

All HHS funded research using newborn dried blood spots must be considered human research regardless of whether the specimens are identifiable.

The IRB may NOT waive informed consent under for research involving newborn dried blood spots for HHS funded research.

For more information, please see *The Newborn Screening Saves Lives Reauthorization Act of 2014*.

**CERTIFICATES OF CONFIDENTIALITY**

Certificates of Confidentiality (CoC) allow researchers to refuse to disclose names or other identifying characteristics of research participants in response to legal demands. Certificates are issued by NIH and other Department of Health and Human Services (HHS) agencies to help protect the privacy of the research participants enrolled in sensitive, health-related research.

A Certificate of Confidentiality helps protect the privacy of research participants enrolled in biomedical, behavioral, clinical and other forms of sensitive health-related research. Certificates protect against compulsory legal demands, such as court orders and subpoenas, for identifying information or identifying characteristics of a research participant. For more information, visit the *NIH Certificate of Confidentiality (CoC) Kiosk*.

Any documents related to processing of the CoC that require the IO signature should go to the Executive Director for review and processing, before they are sent to the IO. The Executive Director will confirm all information is correct, before sending to the IO.

**SPONSORED CLINICAL TRIALS**

Sponsored clinical trials are normally contracted via a comprehensive Clinical Trial Agreement (CTA) which addresses material transfer issues in the CTA or its appendices. When a CTA is reviewed and approved by the Pre-Award office, there may be no need for implementation of an Materials Transfer Agreement (MTA) through DMC’s Office of Technology Commercialization.
Investigators must consult with DMC’s Office of Technology Commercialization to determine whether an MTA is needed in these circumstances and may require additional materials from the PI to ensure safety. When necessary the IRB will obtain an engineering consultant to evaluate the safety of the equipment.

**DEVICE STUDIES**

The PI must provide information in the IRB application to assess whether the investigator or sponsor determined that an IDE is required for a device study, if applicable. Additional supportive documentation is required in the application submission (e.g., letters from the FDA or sponsor).

The IDE regulations (21 CFR 812) apply to all clinical investigations that evaluate the safety and effectiveness of a medical device, unless the criteria for an IDE exemption are met (see IDE exempted investigations).

A medical device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part or accessory that is:

- Listed in the online FDA database,
- Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease, in man or other animals, or
- Intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes [21 U.S.C. 321(h)].

A device that is substantially equivalent to a FDA approved device may have a 510(k) approval to demonstrate the device is safe and effective. Search the FDA 510(k) Database to determine the status of a device in the system.

Studies that involve devices, but that are not designed to evaluate the safety and effectiveness of the device, do not fall under the IDE regulations; however, the IRB still needs to ensure the risks are minimized by using procedures which are consistent with sound research methods or practice and which do not unnecessarily expose participants to risk, and whenever appropriate, by using procedures already being performed on the research participants for diagnostic or treatment purposes. If a device or scientific equipment is not FDA approved for the indicated use in the research, the IRB needs to assess whether it is safe to use in the study.

**IDE EXEMPTED INVESTIGATIONS**
The IDE regulations (21 CFR 812) do not apply to investigations of the following categories of devices:

- A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.
- A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.
- A diagnostic device, if the sponsor complies with applicable requirements in 809.10(c) and if the testing:
  - Is noninvasive,
  - Does not require an invasive sampling procedure that presents significant risk,
  - Does not by design or intention introduce energy into the research participant, and
  - Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
- 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 the research participants at risk.
- A device intended solely for veterinary use.
- A device shipped solely for research on or with laboratory animals and labeled in accordance with 812.5(c).
- A custom device as defined in 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

DETERMINING WHICH DEVICE STUDIES POSE A SIGNIFICANT RISK OR NON-SIGNIFICANT RISK

A significant risk (SR) or non-significant risk (NSR) determination must be made by the sponsor (with concurrence by the IRB) to determine whether an IDE is needed for a medical device study that meets the following criteria:

- The investigation is designed to evaluate the safety and effectiveness of a medical device,
- An IDE has not been issued by the FDA, and
- The study is not exempted.

An IDE is always needed for a SR device study; however, an IRB can review a study that qualifies as a NSR device study (under abbreviated IDE requirements), provided the following:
• The device is not a banned device
• The FDA has NOT notified the sponsor that an IDE is required
• PI maintains the required records and reporting responsibilities to the FDA, 21 CFR 812, Subpart G and complies with the prohibitions against promotion and other practices described in 21 CFR 812.7.

Sponsors are responsible for making the initial risk determination and presenting it to the IRB. The FDA is also available to help the sponsor, PI, and IRB in making the risk determination. Unless the FDA has already made a risk determination for the study, the IRB must review the sponsor's SR or NSR determination for every investigational medical device study reviewed and modify the determination if the IRB disagrees with the sponsor. If the FDA has already made the SR or NSR determination for the study, the FDA’s determination is final.

For more information, see FDA guidance on SR and NSR Medical Device Studies.

RESPONSIBILITIES FOR DEVICE STUDIES

Consult the FDA website on IDE Responsibilities to understand the requirements of Sponsors, Investigators, and Monitors.

DRUGS AND BIOLOGICALS

The following applies to all research involving drugs and biologics:

• Ensure that the research is conducted according to all regulatory guidelines and DMC’s policies and procedures.
• Obtain approval from the IRB before initiating any research activities.
• Comply with DMC’s Investigational Drug/Dispensing and Utilization policy (PHA-11) for storage, security, and dispensing of the drug/biologics, and will be responsible for accounting, return, disposition, and records of accountability per the study protocol.
  o For research conducted at DMC, the PI may delegate the responsibility for drugs/biologics accountability, including storage, dispensing, labeling, and distribution, to the Research Pharmacist (or designee) from the Pharmacy Department.
  o When the above responsibilities are not delegated to the Research Pharmacist, the following must occur:
    ▪ Provide a control plan, to be evaluated by the IRB and ancillary review by the Research Pharmacist (or designee), that includes storage, security, and dispensing of the drugs and biologics and will be responsible for accounting, return, disposition, and records of accountability per the study protocol.
    ▪ Store all drugs/biologics received for a study in a locked environment under secure control with limited access. The area must be within an area of PI’s control. Proper instructions on the use of the drugs/biologics must be provided to the research participants. A log must be kept regarding the
receipt, use, and/or dispensing of the drugs/biologics and the disposition of remaining drugs/biologics after the investigation.

INVESTIGATIONAL NEW DRUG (IND) REQUIREMENTS

When the principle 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) may be required. An IND goes into effect 30 days after the FDA receives the IND request, unless the sponsor receives earlier notice from the FDA.

The PI must provide information in the IRB application to assess whether the investigator or sponsor determined that an IND is required for a proposed study, if applicable. Additional supportive documentation is required in the application submission (e.g., letters from the FDA or sponsor).

Investigators must indicate on the IRB application whether the research involves drugs. If so, they must indicate whether an IND is required for the research. If so, they must provide evidence of the IND, which could be an:

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

The IRB reviewer verifies the IND number is consistent across documents. The IRB is not required to monitor the PI’s performance of required FDA paperwork.

If the research involves drugs and there is no IND, the PI must provide a rationale why it is not required. The IRB review may include a determination as to whether an IND is needed and this determination should be documented in the IRB Minutes. The IRB may ask the PI to request a consultation from the FDA as to whether or not an IND is needed.

If the IRB determines that an IND is needed, final IRB approval will not be granted until one of the following is provided to the IRB:

- Confirmation of an IND number or
- Documentation from the FDA indicating that an IND is not needed.

IND EXEMPTION

The clinical investigation of a drug product that is lawfully marketed in the United States is exempt from the IND requirements if all the following apply:

- The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;
• If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;
• The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
• The investigation is conducted in compliance with the requirements for institutional review and with the requirements for informed consent set forth 21 CFR parts 56 and 50, respectively;
• The investigation is conducted in compliance with the requirements concerning the promotion and sale of drugs (21 CFR 312.7).

**NOTE:** An IND is not needed for a placebo drug or for in vitro testing of a drug.

### RESPONSIBILITIES ASSOCIATED WITH AN IND

• The PI must comply with the [FDA Investigator’s Responsibilities for INDs](http://www.fda.gov/Drugs/InformationOnDrugs/StudyDesign/ucm126589.htm).
• For investigator-initiated IND studies, the PI must comply with [FDA Investigator Responsibilities for Investigator-Initiated IND Applications](http://www.fda.gov/Drugs/InformationOnDrugs/StudyDesign/ucm126589.htm).
• Inform the IRB and the Research Pharmacist when a study involving investigational drugs has been terminated by the sponsor.
• The PI will report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug (21 CFR 312 (b)) according to the procedures in the protocol.

### RESEARCH INVOLVING ENDOGENOUS COMPOUNDS, LIVE ORGANISMS, COSMETICS, DIETARY SUPPLEMENTS, FOOD, FOOD- DERIVED PRODUCTS, SPICES, HERBS, OR ELECTRONIC CIGARETTES

Research using endogenous compounds (e.g., bradykinin, histamine, angiotensin), live organisms (e.g., virus, bacteria, or fungi, whether modified or wild-type), cosmetics dietary supplements, food, food-derived products, spices, herbs, or electronic cigarettes may be an important area of study, particularly, for better understanding, through rigorous scientific investigation, of their mechanisms of actions, pharmacokinetic and clinical effects. Any DMC IRB application which involves these materials must include either proof of an approved IND from the FDA, or a written statement from the FDA certifying that an IND is not needed.

For more information, see the following
• [FDA Draft Guidance on INDs – Determining Whether Human research Studies Can Be Conducted Without an IND](http://www.fda.gov/Drugs/InformationOnDrugs/StudyDesign/ucm126589.htm)
• [FAQs - Clinical Studies Involving Electronic Cigarettes and INDs](http://www.fda.gov/Drugs/InformationOnDrugs/StudyDesign/ucm126589.htm)

### GENE TRANSFER RESEARCH
Gene transfer involves the administration of genetic material to alter the biological properties of living cells for therapeutic use. Gene transfer activities in humans are investigational and are regulated by both FDA and the National Institutes of Health (NIH) Office of Biotechnology Activities (OBA). Prior to IRB approval of a research application and an informed consent involving gene transfer, the following must occur:

- An IND for human gene transfer is required from the FDA,
- The research must be reviewed by U.S. Department of Health and Human Services (DHHS), NIH Recombinant DNA Advisory Committee (RAC), and
- The research must be approved by the IBC.

**RESEARCH INVOLVING MARIJUANA**

Conducting clinical research using marijuana involves interactions with three federal agencies. This includes: obtaining the marijuana for research from the National Institute on Drug Abuse (NIDA) within the National Institutes of Health; review of an investigational new drug (IND) application and the research protocol by the Food and Drug Administration (FDA) and an investigator registration and site licensure by the Drug Enforcement Administration (DEA).

For more information, see the [FDA Guidance on Marijuana research with Human Subjects](#).

**PLANNED EMERGENCY HUMAN RESEARCH OR CLINICAL TRIALS**

Emergency research refers to the study of acute, life-threatening clinical situations. Often, informed consent from the participants is not feasible because the participant lacks the capacity to provide their own consent (e.g., unconscious) and/or there is insufficient time because treatment must be promptly administered. The conduct of planned emergency human research or clinical trials in life-threatening emergent situations requires special consideration by the IRB, including consideration of whether consent may be waived. The specific conditions under which prospective consent of the participant may be waived for planned emergency research are provided by 21 CFR 50.24 and OHRP guidance.

For such research, the IRB will review IRB application materials to ensure the research meets the range of regulatory requirements for emergency research (e.g., community consultation and public disclosure). The IRB must document the required findings outlined below.

The IRB is responsible for the review, approval, and continuing review of the clinical investigation described in this section and may approve that investigation without requiring that informed consent of all research participants be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:

- The research participants are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may
include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

- Obtaining informed consent is not feasible because:
  - The research participants will not be able to give their informed consent as a result of their medical condition;
  - The intervention under investigation must be administered before consent from the research participants' legally authorized representatives is feasible; and
  - There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

- Participation in the research holds out the prospect of direct benefit to the research participants because:
  - Research participants are facing a life-threatening situation that necessitates intervention;
  - Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual research participants; and
  - Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of research participants, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

- The clinical investigation could not practicably be carried out without the waiver.

- The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each research participant within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

- The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with the requirements for informed consent. These procedures and the informed consent document are to be used with research participants or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a research participant's participation in the clinical investigation.

- Additional protections of the rights and welfare of the research participants will be provided, including, at least:
  - Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the research participants will be drawn;
  - Public disclosure to the communities in which the clinical investigation will be conducted and from which the research participants will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;
  - Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;
  - Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and
If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed to, if feasible, attempting to contact within the therapeutic window the research participant’s family member who is not a legally authorized representative, and asking whether he or she objects to the research participant’s participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each research participant, or if the research participant remains incapacitated, a legally authorized representative of the research participant, or if such a representative is not reasonably available, a family member, of the research participant’s inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the research participant, or if the research participant remains incapacitated, a legally authorized representative of the research participant, or if such a representative is not reasonably available, a family member, that he or she may discontinue the research participant’s participation at any time without penalty or loss of benefits to which the research participant is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the research participant’s condition improves, the research participant is also to be informed as soon as feasible. If a research participant is entered into a clinical investigation with waived consent and the research participant dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the research participant’s legally authorized representative or family member, if feasible.

The IRB determinations required above must be documented and are to be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA.

Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include research participants who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists.

If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided above or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

For additional guidance, see:

- [FDA 21 CFR 50.24: Exception from Informed Consent (EFIC) Requirements for Emergency research](https://www.fda.gov/regulatory-information/search-fda-guidance-documents/exception-informed-consent-efic-requirements-emergency-research)
• **FDA Website**: Protection of Human Subjects; Informed Consent and Waiver of Informed Consent Requirements in Certain Emergency research
• **FDA Guidance on Exception from Informed Consent Requirements for Emergency research**
• **OHRP Guidance**: Informed Consent Requirements in Emergency research, for research not subject to FDA regulations

## ENROLLMENT LIST

Upon request, an enrollment list must be made available to the IRB, DMC Leadership, auditors, or government inspectors. At a minimum, this list should include the research participant’s name and also their medical record number, if they are a patient. The list should not be provided to anyone that is not otherwise listed above or in an IRB approved HIPAA instrument. The list may also be used by the IRB, Privacy Officer, or Data Security Officer to notify research participants of possible breaches or concerns that might occur in the research.

**TIP**: If the IRB waives documentation of informed consent, the investigator signature and a witness signature may be included on the enrollment list, when there is IRB approval to enroll cognitively impaired adults or those with limited English proficiency.

## MEDICAL RECORD RESEARCH NOTE FOR CLINICAL TRIALS

When a research participant is enrolled into a **clinical trial involving an IND or IDE** at DMC and is also a **patient**, or when required by the **IRB** (e.g., to help ensure clinicians and pharmacy aware of contraindications), a research note must be placed in the electronic medical record (EMR), unless the IRB determines that it is not in the best interest of the patient or when a Certificate of Confidentiality is appropriate to protect the research participants. When a standard research note is not available in an EMR, the following information must be manually entered by a member of the study team:

- IRB study number
- Study name
- Sponsor
- Principal Investigator
- Main contact information for the study
- Date the patient was enrolled
- Known contraindications
- Anticipated length of study period (years)

For areas that do not use an EMR, the above information must be placed in the beginning of the paper medical records.
External institutions may have their own requirements about research notes; however, they must not be entered into the medical record if the IRB determines that it is not in the best interest of the patient or when a Certificate of Confidentiality is appropriate to protect the research participants.

**LEGALLY EFFECTIVE INFORMED CONSENT AND HIPAA RESEARCH AUTHORIZATION**

**REQUIREMENTS**

Investigators conducting non-exempt human research under the auspices of DMC may involve participants after (s)he or his/her legally authorized representative (LAR), or parent/guardian provides prospective legally effective informed consent/permission (and HIPAA Authorization, when PHI is involved), unless the waiver of such requirements has been approved by IRB.

Assent and (or documentation of assent, when required) of a child or a cognitively impaired adult must also be obtained, unless waived by the IRB.

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

The following procedures describe the requirements for obtaining consent from participants in research conducted at DMC.

**FORM REQUIREMENTS FOR INFORMED CONSENT AND HIPAA RESEARCH AUTHORIZATION**

**TIP:** Informed consent is a “PROCESS,” not just a FORM!!!

This section focuses on the regulatory requirements for the “form.”

Please review additional IRB Guidance on the “process” for obtaining legally effective informed consent and HIPAA Authorization.
Please refer to IRB templates to ensure all required components are included in the document that is submitted to the IRB for approval.

Except as provided elsewhere in this policy, an investigator may not involve a participant in research covered by this policy, unless the investigator has obtained the legally effective informed consent of the research participant or his/her LAR. An investigator shall seek such consent only under circumstances that provide the prospective participant or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the participant or the representative shall be in language understandable to the participant or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the participant or the representative is made to waive or appear to waive any of the participant’s legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

When seeking informed consent, the following basic elements of informed consent shall be provided to each prospective participant (unless waived by the IRB):

- 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;
- A description of any benefits to the research participants or to others which may reasonably be expected from the research;
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the research participant is required if alternatives are available;
- A statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records (if the research is FDA regulated);
- For research involving more than minimal risk, an explanation as to whether there is any compensation for potential study-related injury and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
- An explanation of whom to contact for answers to pertinent questions about the research and research participants’ rights, and whom to contact in the event of a research related injury to the participant;
- A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled, and that the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.
- When seeking informed consent for an “Applicable Clinical Trial”, as defined FDA Amendments Act of 2007 (FDAAA); the following statement must be included in the informed consent documents and should be included in the information sheet, when
documentation of informed consent is waived by the IRB: "A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

When IHII (or PHI) is involved in the study, the required HIPAA authorization language must be included with the informed consent to cover the uses and disclosures of IHII (or PHI). This language is included in the templates in the IRB Application and Reporting System. For additional information see:

- DMC HIPAA-28 Policy: Uses and Disclosures for Research Purposes

When appropriate, one or more of the following additional elements of information must be provided to each research participant:

- A statement that the particular treatment or procedure may involve risks which are currently unforeseeable to the participant (or to the embryo or fetus, if the participant is or may become pregnant);
- Anticipated circumstances under which participation in the research may be terminated by the investigator;
- Any additional costs to the participant that may result from participation in the research;
- The consequences of a participant’s decision to withdraw from the research and procedures for orderly termination of participation;
- 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; or
- The number of participants (approved by the IRB) to be involved in the study. For multi-site studies, it is best to indicate both the number that will be enrolled at the local site and all sites.

**OBTAINING INFORMED CONSENT FROM INDIVIDUALS WITH LIMITED ENGLISH SPEAKING PROFICIENCY**

The information that is given to the research participant or the representative shall be in language understandable to the research participant or the representative.

Unless waived by the IRB, the consent form may be either of the following, as approved by the IRB:

- A written consent document that embodies the elements of informed consent required as outlined above. This form may be read to the participant or the participant’s legally authorized representative, but in any event, the investigator shall give either the participant or the representative adequate opportunity to read it before it is signed; or
• A short form written consent document stating that the elements of informed consent required above have been presented orally to the participant or the participant’s legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary, if the entire consent is not read, of what is to be said to the research participant or the representative. The short form itself is to be signed by the participant or the representative. The witness shall sign both the short form and a copy of the summary (or consent form), and the person actually obtaining consent shall sign a copy of the summary (or consent form). A copy of the summary (if used) and the consent form shall be given to the participant or the representative, in addition to a copy of the short form.

INFORMED CONSENT PROCESS

The IRB evaluates whether or not the informed consent process is adequate and determines whether informed consent is documented and sought in accordance with regulations and policies based on information provided in the IRB application materials, including the IRB application and protocol.

WAIVING THE REQUIREMENTS OF INFORMED CONSENT OR HIPAA AUTHORIZATION

Most prospective human research requires a legally effective informed consent process, including the documentation of a signed consent from the participants; however, when certain criteria are met, the IRB may grant a waiver of the informed consent or pediatric assent requirements. The PI must provide written justification for how the criteria can be met or the IRB can make this determination based on the information available in the protocol or IRB application materials. Requests for waivers of informed consent/assent requirements are not required if the research is considered exempt or if the research does not involve humans, as defined in the regulations; however, a HIPAA waiver or HIPAA Authorization may still be required, for research involving PHI.

There are several types of requests to waive informed consent waiver requirements, as outlined below.

WAIVER OF THE PROCESS FOR INFORMED CONSENT

A request to waive informed consent may be made when the PI wishes to waive the entire process of consent (including documentation). This is generally used for research involving review of retrospective data (i.e., medical charts).

The criteria used for determining whether informed consent can be waived depend on the nature of the research.
For most research, the criteria for waiving informed consent or elements of informed consent are as follows:

1. The research involves no more than minimal risk to the research 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 research participants will be provided with additional pertinent information after participation (e.g., debriefing research participants involved in deception research).

For research or demonstration projects to be conducted by or subject to the approval of state or local government officials (e.g., research approved by the HHS Secretary), the criteria for waiving informed consent or elements of informed consent are as follows:

1. The research or demonstration project is designed to study, evaluate, or otherwise examine:
   a. public benefit or service programs;
   b. procedures for obtaining benefits or services under those programs;
   c. possible changes in or alternatives to those programs or procedures; or
   d. possible changes in methods or levels of payment for benefits or services under those programs; and
2. The research could not practicably be carried out without the waiver or alteration.

**WAIVER OF PARENTAL PERMISSION**

If the IRB determines that a research protocol is designed for conditions or for a population for which parental or guardian permission is not a reasonable requirement to protect the research participants (for example, neglected or abused children), it may waive the consent requirements, provided an appropriate mechanism for protecting the children participating in the research is substituted, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research participants, and their age, maturity, status, and condition.

**WAIVERS OF CHILD ASSENT**

A request to waive child assent may be made when the capability of some or all of the children is so limited that they cannot be reasonably consulted regarding consent. The PI must provide justification for this type of waiver.

A request to waive child assent may be made when the intervention or procedure involved in the research holds out a prospect of direct benefit that is important for the health and well-being of the children, and is only available in the context of an FDA regulated clinical investigation (even if
the IRB determines the children are capable of assenting). The PI must provide justification for this type of waiver, and the following criteria must be met:

- The clinical investigation involves no more than minimal risk to the research participants;
- The waiver or alteration will not adversely affect the rights and welfare of the participants;
- The clinical investigation could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the research participants will be provided with additional pertinent information after participation.
- The permission of the parent(s)/guardian(s) will be documented in accordance with informed consent requirements.

WAIVER OF DOCUMENTATION OF INFORMED CONSENT

A request to waive the documentation of informed consent can be made when informed consent is obtained without documentation (e.g., signed informed consent). When this is requested, the IRB generally requires that an information sheet be provided to the research participant.

A request to waive documentation of informed consent can be approved when the research meets either of the following criteria:

- The research is no greater than minimal risk and involves no procedures for which written consent is normally required outside of the research context, OR
- The only record linking the participant to the research is the consent document and the primary risk would be potential harm resulting from a breach of confidentiality. Under this condition, each participant must be asked whether (s)he wants to sign documentation linking her/him to the research and her/his wishes will govern.

If the study involves PHI, a HIPAA Authorization with a signature must be included, unless a HIPAA alteration (see below) is approved by the IRB. A HIPAA Authorization may be combined with the Information Sheet.

WAIVER OF REQUIRED ELEMENTS OF INFORMED CONSENT

A waiver can be requested to waive certain required elements of informed consent. This is requested when the PI does not wish to include all the required elements in the informed consent document (i.e., cannot disclose purpose of the research, for a project involving deception). The criteria listed to waive the process of informed consent described in this document must be met.

HIPAA WAIVERS

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Uses and disclosures of PHI for research purposes are permitted if the IRB grants HIPAA Waiver (of the HIPAA research authorization requirement). If only a partial HIPAA waiver has been granted, the use or disclosure must be conditioned upon compliance with any HIPAA research authorization requirements that were not waived.

The requested waiver must satisfy all of the following criteria:

- The use or disclosure involves no more than a minimal risk to the privacy of the research participants because:
  - There is an adequate plan to protect the “identifiers” from improper use or disclosure (See Policy HIPAA-6 on De-Identification of Information for the types of information considered to be identifiers;
  - There is an adequate plan to destroy the identifiers at the earliest opportunity, unless there is a health or research justification for retaining the identifiers or their retention is required by law; and
  - There are adequate written assurances that the protected health information (PHI) will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study or for other research for which the use or disclosure of PHI is otherwise permitted.
- The research could not practicably be conducted without the waiver - research involving treatment will almost never be eligible since most clinical trials could practicably be conducted without a waiver; and
- The research could not practicably be conducted without access to and use of the PHI - If de-identified information or a limited data set can practicably be used, a waiver of authorization should not be granted.

The PI should submit the request for waiver using the HIPAA Waiver of Authorization Form. The IRB will review and approve the waiver, if appropriate, under either normal or expedited review procedures. For more information, see DMC Policy HIPAA-28, "Uses and Disclosures for research Purposes."

When the IRB grants a HIPAA waiver, the information in the HIPAA waiver may also be used to grant a waiver of informed consent.

There are three types of HIPAA Waivers (full, partial, and alteration). Each of the types are described below.

**FULL HIPAA WAIVER**

A Full HIPAA Waiver removes the requirement to obtain a HIPAA research authorization from research participants for the use and disclosure of their PHI to conduct a study. Examples where this is appropriate include:

- Retrospective chart reviews
- Exempt research involving PHI, when it is impracticable to obtain a HIPAA research authorization
PARTIAL HIPAA WAIVER

When a Partial HIPAA Waiver is granted to review PHI for recruitment purposes, a HIPAA research authorization is generally required at the time of consent.

HIPAA ALTERATION

A HIPAA Alteration is a type of HIPAA waiver that when approved permits the use of a research authorization that does not contain all of the required elements or statements (e.g., signature or another element), or that otherwise deviates from the format or process prescribed by the HIPAA regulations. This may be useful, for example, when a PI is also seeking waiver of documentation of informed consent, when the only link of a participant to a study is their signature on a consent form and HIPAA research authorization, if it can be considered impracticable to the study’s completion to obtain a signed research authorization form as such a requirement might prevent study completion.

There also may be other circumstances where a simplified consent and authorization document are appropriate given the nature of the population enrolling in the research and in these cases a request to waive certain but not all elements or required statements of the authorization would be made.

DISTRIBUTION OF COPIES OF SIGNED INFORMED CONSENT MATERIALS

The following is a summary of the distribution requirements for informed consent materials:

- Signed Original: research file
- Copies to:
  - Person authorizing the research
  - Medical Record, if clinical trial (unless the IRB determines that it is not in the best interest of the patient or when a Certificate of Confidentiality is obtained)

All original signed and dated forms must be retained in the PI’s research files, secure but readily retrievable. For an FDA regulated clinical trial, the original source document with the original signatures MUST be kept in the research files.

A copy must be provided to the person authorizing the research.

A copy of the signed informed consent document must be filed in the medical record whenever a patient is participating in a clinical trial, unless the IRB determines that it is not in the best interest of the patient or when a Certificate of Confidentiality is appropriate to protect the research participants. If the patient is an outpatient, the document can be filed in the outpatient medical record. The informed consent template may be formatted to be used in the electronic medical record or a copy of the written form can be used.
ANCILLARY REVIEWS

Ancillary reviews by various departments may be required, depending on the nature of the study. To determine if a study requires ancillary review, please see details below or consult the instructions on the IRB application. At the discretion of the IRB, the IRB may consult with others or require ancillary review of a research application at any time.

Ancillary reviewers may request modifications of the research; however, any such modification must also be approved by the IRB.

A conditional approval letter may be issued by the IRB, when a specific type of required ancillary review is pending prior to the final approval of the research; however, a final approval letter cannot be issued until all applicable required ancillary reviews are complete.

For more information, please refer to the instructions on the IRB application form or additional IRB guidance materials.

INSTITUTIONAL REVIEW BOARD (IRB)

The DMC Institutional Review Board (IRB) is a committee established to review and approve human research. The purpose of the IRB is to ensure that all human research be ethically conducted in accordance with all applicable regulations and policy.

The IRB must ensure clinical trials involving investigational or unlicensed test articles (drugs, biologics, and devices) have the appropriate regulatory approval or meet exemptions for such approval and the human research is in compliance with all requirements.

Duties and responsibilities of DMC IRB include, but are not limited to the following:

- Conducting prospective review of human research activities carried out by a DMC faculty member that result in DMC being engaged in human research, regardless of whether the activity is considered a clinical trial, human research, or exempt human research;
- Confirming the competency of the PI;
- Reviewing protocols, investigator brochures, consent forms, advertisements and all other study-related materials submitted to the DMC IRB;
- Reviewing reportable events, as submitted;
- Acting as Privacy Board under 45 CFR Part 164 for research reviewed by DMC IRB and consulting with the DMC Privacy Officer or DMC Data Security Officer, as needed to address relevant matters;
- Maintaining all records of IRB proceedings required by applicable laws and regulations;
- Conducting continuing review of approved studies;
- Reviewing data safety monitoring board reports and taking appropriate actions when needed;
• Reviewing any alleged or suspected incident of noncompliance and making determinations regarding these events;
• Auditing human research, as necessary;
• Providing written standard operating procedures to investigators regarding the process and requirements for IRB application and necessary reporting;
• Making IRB determinations as to whether a DMC activity must be approved by the DMC IRB; and
• Providing relevant IRB Minutes (may be redacted) to an external institution, upon request.

The IRB approves each research protocol or plan according to criteria based on policy, applicable laws, regulations, codes, guidance, and best practices.

IRB CHAIR

The IRB Chair is responsible for seeing that the IRB discharges its functions in an appropriate and regulatory-compliant manner. (S)he holds ultimate responsibility for convening the Board and facilitating meetings, providing to the Institutional Official (IO) recommendations for IRB Membership (including recommendations for pairing primary members with alternates on the IRB roster), and ensuring the IRB operations are in compliance with applicable federal and state statute and regulations. (S)he may delegate some responsibilities to the Vice-Chairs or other experienced IRB Members. The IRB Chair determines whether an activity must be approved by the IRB and determines whether an activity requires IRB review and approval, and whether human research may be reviewed via exempt, expedited, or a full board review process.

The IRB Chair or designate will make determinations regarding events reported to the IRB, or consult with the IRB, IO, Privacy Officer, Information Security Officer, or General Counsel as needed.

IRB VICE-CHAIRS

The Vice-Chairs assist the IRB Chair in carrying out the responsibilities noted in the IRB Chair section and are primarily responsible for the oversight of their designated Full Board meeting. When a Vice-Chair plans to be absent from a full board meeting, the Vice-Chair or IRB Chair may designate an experienced IRB Member to run the meeting, or the IRB Chair will fulfill this duty.

IRB REVIEW PROCESS

Below is an overview of the IRB review process.
PRELIMINARY REVIEW AND REVIEWER ASSIGNMENT

The IRB administrative staff performs a preliminary review of all protocol materials for determination of completeness, accuracy, and required initial signatures (Scientific Review Committee, Department Chair, PI, and any required ancillary reviewers). Only complete submissions can be approved. The PI will be informed through an email of any missing materials or requirements and applicable response deadlines. The IRB administrative staff will assign protocols for review, based on the scientific content of the protocol, the potential reviewer’s area of expertise, and ensure, where applicable, that a scientific and non-scientific perspective is represented. The IRB may use a primary and secondary reviewer process (e.g., two reviewers), or assign reviews based on special knowledge and expertise of the members (e.g., clinical expertise, informed consent reviewer, research design, statistics, regulatory and policy, ethics) or a combination thereof. When the IRB is presented with a protocol that may be outside of the knowledge base of any of the IRB, an outside consultant will be sought. Protocols for which appropriate expertise cannot be obtained for a given meeting may be deferred to another IRB committee or an external IRB.

At least one IRB Member will be assigned to a study that qualifies for an exemption or expedited review. At least two reviewers will be assigned to each full board protocol and a reviewer may be assigned several protocols or other research items for review. Reviewers are assigned to all protocols requiring initial review, continuing review, and modifications. In general, the reviewers are responsible for the following:

- Having a thorough knowledge of all of the details of the proposed research;
- Performing an in-depth review of the proposed research and all uploaded documents;
- Leading the discussion of the proposed research at the convened meeting, presenting both positive and negative aspects of the research, and leading the IRB through the regulatory criteria for approval;
- Making suggestions for changes to the proposed research, where applicable;
- Completing all applicable IRB reviewer forms or placing comments in the electronic IRB submission and reporting system.

All reviews must be completed in writing in the electronic IRB submission and reporting system, including IRB determinations; however, the reviews are not considered the final work product of full board studies. The final review for the full board will be determined by the information discussed at the meeting, including any additional determinations, and captured in the IRB minutes and IRB approval/notification letters.

PROCESS FOR EXEMPT, EXPEDITED, OR FULL IRB REVIEW

All human research requires, based on the criteria set forth below, either full review, expedited review, or exempt review. An investigator may propose the type of review; however, the IRB makes the final determination.
When a new study is submitted the IRB Office staff will review the materials to see if the study qualifies for exempt, expedited, or full board review. If there are any questions, the IRB staff will consult with the Executive Director, Vice-Chair, or IRB Chair for guidance or a determination.

If a project does not need IRB review and approval, the IRB will issue a determination letter to this effect.

**EXEMPT RESEARCH REVIEW PROCESS**

Exemption requests are reviewed as they are submitted. There are no scheduled deadlines for submission, as the review process will start immediately.

The IRB office staff will conduct an administrative review of the research to determine whether the submission is complete and verify the study meets the criteria for an exempt review. If the IRB office staff member is also an experienced IRB Member and has the expertise necessary to conduct the review, (s)he may review and approve the research; otherwise, it will be assigned to another IRB Member.

The IRB Member may require additional changes or make recommendations before approving the study. The IRB Member can refer the study to the IRB Chair or another IRB Member, if the topic is out of his/her area of expertise. An IRB Member cannot disapprove the research, but may refer it to expedited or full board review.

**EXPEDITED REVIEW PROCESS**

Expedited review of a new study or continuing review of a previously IRB approved study entails designated review by the IRB Chair and/or a designated IRB Member (s) in lieu of a convened (full) IRB review and thus may shorten the time to approval; however, the project must still meet all requirements. There are no scheduled deadlines for submission, as the review process will start immediately.

An experienced IRB Member will review and may approve the research package. The IRB Member may require additional changes or make recommendations before approving the study. The IRB Member can refer the study to the IRB Chair, Vice-Chair or another experienced IRB Member, if the topic is out of their area of expertise. An IRB Member cannot disapprove the research, but they can defer it to full board review.

The IRB Chair has final approval authority, if there are any concerns. The IRB Chair cannot disapprove a project under the expedited review process, but may defer it to the convened IRB for a final decision.
EXPEDITED REVIEW OF AMENDMENTS, CONTINUING REVIEW (PROGRESS REPORTS), REPORTABLE EVENTS, AND OTHER CONSIDERATIONS

Review of amendments, continuing review (progress reports), reportable events, and other considerations, shall be done via expedited review whenever permissible under the regulations. An experienced IRB Member will confirm the study qualifies for expedited review. An experienced IRB Member conducting the review may approve the research submission. The IRB Member may require additional changes or make recommendations before approving the submission. The IRB Member can refer the study to the IRB Chair, Vice-Chair or another experienced IRB Member, if the topic is out of his/her area of expertise. An IRB Member cannot disapprove the research, but they can defer it to full board review for approval or acknowledgement.

SERIOUS ADVERSE EVENT (SAE) REVIEW PROCESS

An experienced IRB Member will review and may approve the SAEs or reportable event by expedited review. The IRB Member may require additional information, request changes to the research or make recommendations before approving the SAE. The IRB Member can refer the study to the IRB Chair, Vice-Chair, another experienced IRB Member, of the Full Board if the topic is out of their area of expertise.

FULL (CONVENED) IRB REVIEW PROCESS

It is the responsibility of the PI to submit all required materials and signatures according to the posted schedule on the IRB website prior to a scheduled IRB meeting, unless special extenuating circumstances are approved by the Executive Director, Vice-Chair, or IRB Chair.

PRE-MEETING DISTRIBUTION OF DOCUMENTS

The meeting agenda will be prepared by the IRB administrative staff and made available to the IRB Members prior to the meeting. All IRB Members receive access to agenda and all submission materials, approximately five (5) business days before the scheduled meeting to allow sufficient time for the review process. Prior month’s meeting IRB Minutes, applicable business items and audits, and appropriate continuing education materials will be made available approximately five (5) business days before the scheduled meeting, if feasible. Exceptions for late submissions may be approved by the IRB Chair, Vice Chair, or Executive Director. Appropriate IRB Members will be assigned by the IRB Chair (or designate) to be reviewers on one or more of the applications.

All of the IRB Members receive and are expected to review all studies, not just the ones they are assigned to review.
INVESTIGATOR ATTENDANCE

To improve efficiencies and communication the PI for any new study undergoing initial review by the full committee is invited to attend to present the study and answer any questions of the IRB. It is in the best interest of the PI to attend or call into the meeting. Study team members may also attend with or on behalf of the PI; however, if questions cannot be answered, the IRB may need to disapprove the study or require additional modifications or clarifications in order to grant final approval.

IRB ATTENDANCE, QUORUM, AND VOTING

By regulation, final action on protocols that require full IRB review may be taken only at a convened meeting. The convened meetings are generally held on the first (Committee A) and third (Committee B) Wednesday of each month. Committee E meetings may be called by the IRB Chair or Vice-Chair for emergency or otherwise critical reviews.

A necessary quorum for the IRB to consider a proposal is a majority of the total number of primary members for the Committee, including a member whose primary concern is in a non-scientific area, before regulatory actions may be taken at these meetings. See section on IRB Minutes for additional information. If research involving an FDA-regulated article is involved, a licensed physician must be included in the quorum. A quorum must be present before a vote can take place. Members must be present in person or via teleconference or video conference.

All members receive all pertinent material prior to the meeting and are considered present when they actively and equally participate in all discussions through teleconferencing or videoconferencing.

Advanced (proxy) votes are not permitted for voting on regulatory actions that are required during a convened IRB meeting; however, an IRB Member may record their recommendations in the electronic IRB submission and reporting system in advance of the meeting. Voting for non-regulatory required actions (e.g., approval of IRB Minutes or other business related decisions), may take place via e-mail or phone.

No IRB may have a member participate in the board's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB. An IRB Member with a potential or real conflict of interest will be required to abstain from voting on the project. The conflicted member will leave the room during discussion and voting, if required by the IRB Chair or Vice Chair. The abstention and absence, if applicable, will be noted in the IRB meeting IRB Minutes.

At the convened meeting each submission is discussed. A vote is taken after a motion is made.

If an IRB Chair or Vice-Chair entertains a motion under which the IRB votes on groups of studies (sometimes called “block voting”), IRB Members have the ability to voice their vote “for” on some studies, “against” on others, and “abstain” on others.
If all of the reviewers are absent from the meeting, the IRB Vice Chair will determine if the study in question must be tabled for a review at a future meeting; if the present members have sufficient information and expertise, then review will proceed.

**RISK ASSESSMENT AND MINIMIZATION**

At the time of initial and continuing review, the IRB will make a determination regarding the risks associated with the research protocols and whether risks can be minimized through appropriate measures. Risks associated with the research will be classified as either "minimal" (no greater than minimal risk) or "greater than minimal" based on the regulatory definitions of minimal risk. The level of risk is entered in the electronic IRB submission and reporting system.

In order for research involving children to meet the criteria for approval under category 406 (45 CFR 46.406 or 21 CFR 50.53), the IRB must determine that the research risk represents only a minor increase over minimal risk.

IRBs should verify or make the SR or NSR determination of an investigation involving the safety and effectiveness of a medical device by reviewing relevant information at a convened meeting.

**ASSESSMENT OF BENEFITS**

The IRB assesses the potential benefits of the research to the research participants and society, based on the IRB application materials and experience of the IRB. The IRB considers whether the benefits that may be reasonably expected to result provide a reasonable basis for assuming the risks of the research.

Compensation and reimbursement is NOT considered a benefit.

**DETERMINING WHICH PROJECTS REQUIRE REVIEW MORE OFTEN THAN ANNUALLY**

At the time of initial review and at continuing review, the IRB will make a determination regarding the frequency of review of the research protocols. All protocols will be reviewed by the IRB at intervals appropriate to the degree of risk but no less than once per year. In some circumstances, a shorter review interval (e.g., biannually, quarterly, or after accrual of a specific number of participants) may be required. The expiration date of the approval period will be entered in the electronic IRB submission and reporting system and the approval letter will reflect the expiration date.
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 research participants either studied or enrolled. If a maximum number of research 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 research participants studied or enrolled determines the approval period only when that number of research participants is studied or enrolled in less than one year.

Most research projects will be granted a one-year review period unless otherwise specified by the IRB. The following factors will be considered when determining which studies require review more frequently than on an annual basis:

- Significant risk to research participants (e.g., death, permanent or long lasting disability or morbidity, severe toxicity) with the possibility of direct benefit to the research participants;
- The inclusion of significantly vulnerable populations where, even in the presence of possible direct benefit, there is also a possibility of significant risk associated with the research procedures.
- The probability and magnitude of anticipated risks to research participants.
- The likely medical condition of the proposed research participants.
- The overall qualifications of the PI and other members of the research team.
- The specific experience of the PI and other members of the research team in conducting similar research.
- The novelty of the research making unanticipated adverse events more likely.
- The nature of any risks posed by the research project.
- The degree of uncertainty regarding the risks involved.
- The vulnerability of the research participants' population.
- The experience of the investigators in conducting research.
- The IRB's previous experience with the investigators (e.g., compliance history, previous problems with the investigator obtaining informed consent, or prior complaints from research participants about the investigator);
- The projected rate of enrollment.
- Whether the research project involves novel interventions.
- Any other factors that the IRB deems relevant.

**DETERMINING EFFECTIVE DATE OF INITIAL IRB APPROVAL AND DATE FOR CONTINUING REVIEW**

The IRB follows [OHRP Guidance on Continuing Review](https://www.hhs.gov/ohrp) and the [FDA Guidance on Continuing Review](https://www.fda.gov) for determining the effective date of initial IRB approval and the dates for continuing review.

In general, continuing review is not required for exempt research, unless the IRB determines otherwise and provides and expiration date for the IRB approval.
When the IRB reviews and approves research via expedited review, the effective date of the initial approval is the date on which an experienced IRB Member has reviewed and accepted as satisfactory the protocol or informed consent documents, or any other responsive materials, required by the IRB from the investigators. In such circumstances, the expiration date of the initial approval period, which is the date by which the first continuing review must occur, may be as late as one year after that effective date of initial IRB approval.

When the IRB reviews and approves research *with conditions* at a convened IRB meeting without requiring further review at a subsequent convened meeting, the effective date of the initial approval is the date on which the IRB Chair or an experienced IRB Member has reviewed and accepted as satisfactory all changes to the protocol or informed consent documents, or any other responsive materials, required by the IRB from the investigators. In such circumstances, the expiration date of the initial approval period, which is the date by which the first continuing review must occur, may be as late as one year after that effective date of initial IRB approval. However, the IRB may choose to set the expiration date of the initial approval period at one year from the date of the IRB meeting at which the research project initially was approved with conditions.

Please see the OHRP and FDA guidance referenced above for specific examples of various scenarios.

When a study is reviewed and approved by an external IRB, the DMC IRB will acknowledge the expiration date determined by the external IRB.

**VERIFICATION THAT NO MATERIAL CHANGES HAVE OCCURRED**

The IRB recognizes that protecting the rights and welfare of research participants sometimes requires that the IRB obtain independent verification, utilizing sources other than the investigators that no material changes occurred during the IRB-designated approval period. Independent verification from sources other than the investigator (e.g., auditor, IRB, sponsor, or other third party) may be necessary at times, for example, in cooperative studies, or other multi-center research.

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

- Protocols where concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources
- Protocols conducted by a PI who has previously failed to comply with federal regulations and/or the requirements or determinations of the IRB
- Protocols selected for internal audit
- Whenever else the IRB deems verification from outside sources is relevant
- The probability and magnitude of anticipated risks to research participants
- The likely medical condition of the proposed research participants
• The probable nature and frequency of changes that may ordinarily be expected in the type of research proposed

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

Following the monitoring, a report of the findings will be submitted to the IRB, which will determine the appropriate action to be taken.

CONSENT MONITORING

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

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

Such monitoring may be particularly warranted for:

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

If the IRB determines that consent monitoring is required, the monitoring may be conducted by IRB administrative staff, IRB Members or another party, either affiliated or not with the institution. The PI will be notified of the IRB’s determination and the reasons for the determination. Arrangements will be made with the PI for the monitoring of the consent process for a specified number of research participants. When observing the consent process, the monitor will determine:

• Whether the informed consent process was appropriately completed and documented,
• Whether the research participants had sufficient time to consider study participation,
• Whether the consent process involved coercion or undue influence,
• Whether the information was accurate and conveyed in understandable language, and
• Whether the research participants appeared to understand the information and gave their voluntary consent.

Following the monitoring, a report of the findings will be submitted to the IRB, which will determine if any actions are required.

STAMPING REQUIREMENTS OF IRB APPROVED MATERIALS

The following IRB approved documents MUST be stamped by the IRB with a valid date range before they can be used for recruitment and enrollment for each research study:
• Long Forms (informed consent documents, HIPAA research authorizations, information sheets, assent Documents), including addendums
• Short Forms
• Summaries of what will be said to a potential research participant
• Oral consent or recruitment scripts
• Recruitment posters, advertisements, or flyers (if technically feasible)

The study staff must check the data stamp on the informed consent materials, before enrolling research participants to make sure the most current forms are used.

If any of the above documents have been translated into languages other than English, they will receive an IRB stamp, after the translated materials are approved by the IRB.

The documents may be stamped by the IRB Office Staff.

The stamp will include the study number, package number, approval date and study’s expiration date. However, the study’s expiration date will only appear on the approved Long Forms or Short Forms.

For the other study documents, the stamp will include the study number, package number and approval date.

The stamped documents will be published in the electronic IRB submission and reporting system and the PI and anyone who has access to the submission will receive an e-mail notice that the document is available.

If it is not feasible to stamp recruitment materials with IRB stamp (i.e., newspaper and electronic advertisements), posting of the document is permitted without the stamp as long as there are no modifications to the IRB approved language in the material, and the IRB approval letter references the approved materials.

The IRB does not stamp the following documents after they are approved; however, an IRB approval letter listing these materials must be on file with the investigator, before they can be used:
• Surveys
• Recruitment letters
• Other recruitment materials and documents that are not mentioned above
• IRB applications
• Protocols
• Study brochures
• Investigator Brochures (IB)
• Case report forms
• Data collection tools
• Scales and questionnaires/surveys
• Sponsor correspondences
• IND safety reports

**IRB LETTERS AND NOTIFICATIONS**

Once the research is approved, the PI will receive a letter of approval. Once approved by the IRB, research may be only conducted within the policies and procedures outlined by the IRB and within the constraints of other institutional and federal requirements. IRB approval does not in itself constitute administrative approval to initiate the research project, as additional requirements may also apply, before the research may begin (e.g., Pre-Award approval, Contract approval, STAR approval for NYC H+H Kings County research, etc.).

Once an IRB Member completes his/her review (expedited/exempt) or after a full board meeting, the IRB Office will generate a letter to the PI dependent on the decision of the IRB. The letter is generated in the electronic IRB submission and reporting system. The selected letter depends on the decision of the IRB. Once the letter is generated, the IRB Office may notify the assigned Expedited reviewer (through committee messages in the electronic IRB submission and reporting system) if the letter needs to be reviewed for any clarification or feedback (e.g. adding notes or requirements from the IRB), if needed. The IRB member conducting the review may edit and publish the letter.

The letters for expedited and exempt reviews will be published in the electronic IRB submission and reporting system by an IRB office staff member or by an IRB member when they are deemed by the expedited reviewer to be suitable for issuance.

Full board letters must be reviewed by the IRB Vice-Chair for the specific committee relevant to the review, or by the Executive Director, Human research Protections and Quality Assurance. The Vice-Chair or Executive Director makes any necessary edits and notifies the IRB Chair of the IRB that the letter is ready for review. The Chair (or designate) will review and make any final edits that may be needed, before publishing the letter.

In general, the goal of the IRB is to publish letters within 5 days of the IRB’s determination; however, this may be adjusted based on workload and staffing. If a letter is needed and it has been 5 days past the date of IRB approval, the research team may contact the IRB to escalate the request. When the letters are published in the electronic IRB submission and reporting
system, the PI and anyone who has access to the submission will receive an e-mail notice that the letter is available.

In general, the investigators are expected to respond within the following timeframes, or the submission is considered withdrawn:

- The research team will have **2 weeks** to respond from the date of that notification letter to any IRB requests regarding missing documents, training or signatures for all initial IRB Submissions including Exempt, Expedited and Full Board studies.
- The research team will have **1 month** to respond from the date of a modification letter from the IRB requesting MINOR changes or a letter of conditional approval.
- The research team will have **2 months** to respond from the date of IRB notification letter regarding MAJOR changes.

### POSSIBLE IRB ACTIONS OR APPROVALS

The following possible IRB Actions or Approvals are entered in the IRB application and submission system and are included within the IRB letter.

#### APPROVED

The research study is approved as submitted without any conditions or required modifications. The IRB may also elect to make changes in order to secure approval, provided the PI is also notified of the changes the IRB made in order to secure approval.

If the IRB makes a motion for approval at the convened meeting when the actions requested require conditional approval or modifications based on regulations or policy, the IRB will issue a Conditional Approval or Modifications Required letter, as applicable to the action required.

#### ACKNOWLEDGEMENT

The IRB acknowledges the receipt of the submitted materials. No additional actions are usually required, unless specified in the IRB letter.

#### APPROVED WITH CONDITIONS

The research is approved with conditions. When minor and specific changes are required, the IRB notifies the PI in writing of the changes that are required. The IRB may approve research with conditions if, given the scope and nature of the conditions, the IRB is able, based on the assumption that the conditions are satisfied, to make all of the determinations required for
approval under the regulations. For example, the IRB may require the following as conditions of approval of research:

- Confirmation of specific assumptions or understandings on the part of the IRB regarding how the research will be conducted (e.g., confirmation that the research excludes children);
- Submission of additional documentation (e.g., certificate of CITI training);
- Precise language changes to protocol or informed consent documents; or
- Substantive changes to protocol or informed consent documents along with clearly stated parameters that the changes must satisfy.

For more specific information, please refer to the OHRP guidance on Approval of research with Conditions and FDA Guidance on IRB Continuing Review after Clinical Investigation Approval.

If the IRB makes a motion for conditional approval at the convened meeting when the actions requested require modifications based on regulations or policy, the IRB will issue a Modifications Required letter.

**FINAL APPROVAL**

When the PI responds to the conditional approval request, the changes are reviewed by an IRB Member by expedited review, to confirm the changes were made as directed, before final approval is granted.

**MODIFICATIONS REQUIRED**

When the Full Board requires modifications, the request for changes will be provided in writing to the PI, which must be returned to full board review. In general, whenever the scientific design or merit is questioned, or when major modifications are requested, the IRB may also return the project to the SRC, as determined by the IRB Chair, Vice-Chair, or convened IRB.

When modifications are required of a study which qualifies for expedited or exempt review, the returned modifications will be reviewed by an expedited process.

**DISAPPROVED / NOT APPROVED**

When research is disapproved, the PI will be notified in writing of the reasons. When a study is disapproved, the Department Chair and the SRC must also be notified.

**DEFER / TABLED**
The IRB Chair or Vice-Chair can defer or table a study to a future meeting or another committee, with or without the majority vote of the IRB, for any of the following reasons:

- The IRB is unable to review the submission for any reason;
- The Chair or Vice-Chair elect to defer the research when it is need of substantive changes before it can be presented to the IRB;
- Loss of quorum; or
- Lack of expertise on one of the IRB Committees

If applicable, the IRB will provide a written summary of any concerns that have been submitted by any of the reviewers at the time of notification. The Department Chair and/or the SRC may also be notified, particularly if substantial revisions are required or when a submission cannot be evaluated.

The IRB will re-review the submission (or revised submission) at a future meeting.

**WITHDRAWN SUBMISSION**

The PI may withdraw a submission at any time; however, the IRB may also administratively withdraw a submission as needed.

When an IRB submission is incomplete and/or for which changes are requested, the IRB administrative staff will inform the PI which items, documents, and/or modifications are still needed in order to complete the review. If a response from the PI is not received within the specified time frame the submission will be administratively withdrawn from consideration.

Once it has been administratively withdrawn due to lack of response, the review may be continued only upon receipt of a response addressing any concerns raised in the initial review. The new material will then be reviewed by the IRB.

**CLOSED**

When the IRB acknowledges a closure or final report, the IRB will issue a letter to this effect. The IRB may also issue a closure letter when a study expires.

**EXPIRED**

When the IRB approval period of a study expires, the electronic IRB submission and reporting system issues an e-mail stating such.
SUSPENSION OR TERMINATION

When the IRB is notified that a study is suspended or terminated, the IRB will acknowledge such. If the IRB suspends or terminates IRB approval, the letter will state such actions.

NOT HUMAN RESEARCH

When the DMC IRB determines an activity does not meet the requirements for human research a letter will be issued stating such. DMC IRB approval will not be required.

NOT ENGAGED IN HUMAN RESEARCH

When the DMC IRB determines the DMC workforce is not conducting activities which make DMC engaged in human research, a letter will be issued stating such. DMC IRB approval is not required.

IRB MINUTES

Minutes are taken at all IRB meetings. Minutes of IRB meetings shall be in sufficient detail to show attendance at the meetings; quorum; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

Any items approved outside of the full board meetings, will be included in the IRB Minutes to notify the board members of all such actions.

DISTRIBUTION OF IRB MEETING MINUTES

Copies of the approved IRB Minutes are distributed as follows:

- Medical Board Office for the Medical Executive Committee
- Institutional Official
- Executive Director, Human Research Protections

Relevant redacted minutes are available upon request to external institutions. The IRB Chair, Vice-Chair, or the Executive Director must review the redacted minutes before they are distributed to an external institution.
POST IRB APPROVAL

GENERAL REQUIREMENTS

The study team should do the following after a study is approved by the IRB:

- Review the IRB approval letter for accuracy and appropriate determinations.
- Check the approval date and expiration date in letter and approved documents (consent, recruitment materials, etc.). An expiration date is NOT needed for recruitment materials.
- Contact the IRB if there are any discrepancies, errors, or questions.
- Share applicable documents with sponsor.
- File documents in study binder.
- Ensure Applicable Clinical Trial Requirements are made as required by FDA.
- Understand and ensure the requirements of sponsor.
- Understand reporting requirements to the IRB, sponsor, and FDA.
- Ensure that laboratory reports from research laboratories are not used for diagnosis, treatment and prevention of disease, unless the research laboratory is properly certified or accredited.

REPORTABLE EVENTS

All required reportable events must be reported to the IRB within the deadlines specified in the table below. Please see definitions in IRB guidance materials for clarification of the event type or contact the IRB.

When reviewing any reportable event, the IRB may consider, but is not limited to, the following possible actions:

- Modification of the protocol
- Modification of the consent document or process for obtaining consent
- Modification of the information disclosed during the consent process
- Providing additional information to current participants (This must be done whenever the information may relate to the participant’s willingness to continue participation)
- Providing additional information to past participants
- Requiring current participants to re-consent to participation
- Alteration of the frequency of continuing review
- Observation of the research or the consent process
- Requiring additional training of the investigator
- Notification of investigators at other sites
- Termination or suspension of IRB Approval
- Referral to other organizational entities
- Obtaining additional information
- Taking no action
Before a hold, termination, or suspension is put into effect by the IRB, the IRB Chair, or IRB Vice-Chair considers whether any additional procedures need to be followed to protect the rights and welfare of current participants. Such procedures might include:

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

<table>
<thead>
<tr>
<th>Event Type</th>
<th>Deadline from when the investigator first learns of an internal event for reporting to IRB for an internal event (e.g., those that occurred within the DMC IRB’s jurisdiction)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Government inspection (or audit)</td>
<td>Report findings within 24 hours, if any serious or continuing non-compliance was found or proposed; otherwise within 5 days.</td>
<td>The study team should alert the IRB when the inspection is scheduled or if an inspector arrives unannounced, so the IRB may help as needed.</td>
</tr>
<tr>
<td>*Privacy Violation (or Breach)</td>
<td>Immediately report this to IRB and Privacy Officer</td>
<td></td>
</tr>
<tr>
<td>*Information (Data) Security Violation (or Breach)</td>
<td>Immediately report this to IRB and Data Security Officer</td>
<td></td>
</tr>
<tr>
<td>Incarceration of a research participant.</td>
<td>Immediately, if participant is actively incarcerated; otherwise within 5 days</td>
<td></td>
</tr>
<tr>
<td>Any FDA Actions or changes to a HUD.</td>
<td>Immediate</td>
<td></td>
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</tbody>
</table>
### Serious Adverse Event.

An AE or SAE may also meet the definition of an UPIRPO, UAE, or UADE, as described below.

24 hours, if in a Clinical Trial an internal AE meets the following criteria:

- serious (or alarming) AND
- unanticipated (unexpected), AND
- would have implications for the conduct of the study (e.g., requiring a significant, and usually safety-related, change in the protocol such as revising inclusion/exclusion criteria or including a new monitoring requirement, informed consent, or investigator’s brochure).

The term “alarming” is not defined by the FDA, so it is up to the PI’s or Sponsor’s discretion on how to interpret this term.

An individual AE occurrence ordinarily does not meet these criteria because, as an isolated event, its implications for the study cannot be understood.

Reporting requirements to the sponsor of AEs for clinical trials conducted under IND are stricter. Consult with the sponsor or see FDA Guidance on AE reporting to the IRB.

| *Research related injury involving provision of healthcare.* | 24 hours, if serious. | The PI or IRB may consult with general counsel regarding recommended action. |
| *Apparent Non-Compliance.* | 24 hours, if serious or continuing | Any employee or agent is expected to report any apparent non-compliance to the IRB or to the Compliance Hot Line at 877-349-SUNY (7869) or via the Web-based Reporting Compliance Line. You may make an anonymous report using the web based system, if desired. |
| New Information that Indicates a Change to the Risks or Potential Benefits of the Project. | 24 hours if serious; otherwise within 5 days |  |
| Significant New Finding. | If serious, notify the IRB within 24 hours; otherwise, submit to the IRB within 30 days of notice | During the course of research, significant new knowledge or findings about the medication or test article and/or the condition under study may develop. The PI should report any significant new findings to |
the IRB and the IRB will review them with regard to the impact on the research participants’ rights and welfare. Since the new knowledge or findings may affect the risks or benefits to research participants’ willingness to continue in the research, the IRB may require, during the ongoing review process, that the PI contact the currently enrolled research participants to inform them of the new information. If the change to the risk/benefits ratio is adverse, the informed consent should be amended and submitted to IRB for approval. The informed consent should be updated and the IRB may require that the currently enrolled research participants be re-consented, acknowledging receipt of this new information and for affirming their continued participation.

<table>
<thead>
<tr>
<th>Changes Initiated to Eliminate an Apparent Immediate Hazard</th>
<th>5 days</th>
<th>Include an amendment, to propose any additional or permanent changes.</th>
</tr>
</thead>
<tbody>
<tr>
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<td>5 days</td>
<td>Include an amendment, to propose any additional or permanent changes.</td>
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<td>5 days</td>
<td>Include an amendment, to propose any additional or permanent changes.</td>
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</table>

| Protocol Deviations (including minor modifications made without IRB approval), Violations, or Complaints. | 5 days, if it adversely affects: the rights, safety, or welfare of the research participant; or the research participant’s willingness to continue participation; or the integrity of the research data, including information security | Include an amendment, to propose any additional or permanent changes, as a corrective action. |

Any complaints involving translations or interpretations must also be reported to
<table>
<thead>
<tr>
<th>Event Description</th>
<th>Reporting Requirements</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Termination or Suspensions of research, Administrative Hold, FDA Clinical Hold, Enrollment Hold.</td>
<td>5 days</td>
<td>The IRB may also elect to terminate or suspend IRB approval or place enrollment on hold, and all such actions require reporting to OHRP, and to FDA and sponsor when applicable, by the IO.</td>
</tr>
<tr>
<td>All Local Unanticipated Problems Involving Risks to Participants or Others (UPIRPO).</td>
<td>5 days, if serious; otherwise, within 30 days</td>
<td>If the IRB concurs or determines that an event is an UPIRPO, it requires reporting by the IO to the OHRP, and to FDA when applicable.</td>
</tr>
<tr>
<td>Unexpected AE (UAE). See also SAE and UPIRPO.</td>
<td>5 days, if serious; otherwise, within 30 days</td>
<td>If the IRB concurs or determines that this event is also an UPIRPO, it requires reporting by the IO to the OHRP, and to FDA when applicable.</td>
</tr>
<tr>
<td>Audit or Monitoring Activities. *Must be reported to the full board if the event meets the requirements to be reported within 5 days.</td>
<td>5 days if findings identify apparent serious or continuing noncompliance; otherwise at continuing review or study closure.</td>
<td></td>
</tr>
<tr>
<td>Unanticipated Adverse Device Effect (UADE). See also SAE and UPIRPO.</td>
<td>As soon as possible, but no later than 10 days</td>
<td>Report to sponsor within 10 days. If the IRB concurs or determines that this event is also an UPIRPO, it requires reporting by the IO to the</td>
</tr>
<tr>
<td>Event Type</td>
<td>Submission/Reporting Requirements</td>
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<td>---------------------------------------------------------------------------</td>
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<td>Interim Analysis Reports, Data Monitoring Committee Data and Safety Monitoring Board (DSMB) reports.</td>
<td>Submit to the IRB within 30 days of notice</td>
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<tr>
<td>External reportable events (e.g., those that occurred with participants that were enrolled outside of the local site of the IRB jurisdiction).</td>
<td>N/A</td>
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<tr>
<td>Sponsored required reporting.</td>
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</table>

When indicated, call the IRB at (718) 613-8480.

To report any events in writing, please do so in the electronic IRB submission and reporting system, using the Reportable Event Form.

The items listed in the table above with an "*" next to the event type must be reviewed at the full board. In general, all other reportable events will be reviewed by an expedited reviewer; however, any clinical event must be reviewed by at least one IRB Member who is a clinician. The reviewer may consult with other IRB Members when conducting the review or defer the review to the full board at any time.

**AMENDMENTS**

Any proposed changes to non-exempt human research must be submitted to the IRB. Changes to exempt research must be submitted to the IRB, if the changes meet the criteria outlined in the following subsection.

**IMPORTANT:** Federal regulations require prompt reporting to the IRB of proposed changes in a research activity. Do not wait until the time of Continuing Review to request approval of an amendment. Changes in approved research may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards or to protect the life or physical well-being of the research participant.

The IRB Office, in consultation with the IRB Chair when needed, will determine if the amendment can be expedited (i.e., minor changes, additional research staff, no change to risk/benefit ratio, etc.) or whether it needs to be reviewed by the full board (more than minor changes, increase in risk/benefit ratio, etc.).
The following are examples of changes that are considered minor and may be expedited:

- Adding or removing research staff
- Making changes that do not affect the risks of the research or the risks/benefit ratio
- Administrative corrections or clarifications
- Non-substantial changes in the research design or methodology
- A proposed change in the number of research participants enrolled in the research
- Multiple minor changes

The following examples are of changes that must go to the full board:

- A change in the qualifications of the research team
- A change in the facilities available to support the safe conduct of the research
- Any other factor that may increase the risk to research participants or others

Addition of study staff always requires an amendment, prior to the study staff conducting any research, including research that was approved as exempt. Relevant COI disclosures and training requirements must be submitted with the amendment, if the documentation is not on file with the IRB.

An amendment may not necessarily need to be promptly reviewed and approved by the IRB, when a change is necessary to eliminate apparent immediate hazards or to protect the life or physical well-being of the research participant; however, such a change must be reported to the IRB within 5 business days. If an amendment is needed to prevent a future hazard or protect the life or well-being or research participants, the amendment must be promptly submitted to the IRB.

The PI signature is always required for an amendment; and the Department Chair’s signature required if there is a change in the PI.

Although an amendment may be processed at the time of continuing review it is recommended the amendment be submitted to the IRB as a separate event as soon as the change is needed, so the reviews do not interfere with one another.

All amendment requests must be submitted in the electronic IRB submission and reporting system. The instructions are included on the Amendment request form and include a list of required materials needed for the amendment.

Whether or not the amendment includes changes to an IRB-approved informed consent form, the IRB will review the amended or current informed consent document carefully to determine if it requires any additional revisions based on the submitted amendment, current IRB policy and practices, and current informed consent templates.

In general, expedited amendments will be reviewed by an expedited reviewer; however, any clinical event must be reviewed by an IRB Member who is a clinician. The reviewer may consult
with other IRB Members when conducting the review or defer the review to the full board at any time.

**CHANGES IN EXEMPT RESEARCH**

Most changes to exempt research do not need to be approved by the IRB; however, an amendment must be submitted to the IRB for prospective approval, prior to the initiation of the change, for any of the following reasons:

- reporting a new or revised Significant Financial Interest in a conflict of interest disclosure for any who is considered an investigator for the purposes of COI, for a federally funded or supported research study,
- proposed change in investigative staff,
- proposed change to the research that places the research under it in a different exempt category, or
- proposed change to the research that requires a higher level of review (e.g., expedited or full board review).

If the proposed changes to exempt research require expedited review, please contact the IRB to determine if an expedited IRB application form is required, as additional information may be required.

**ACKNOWLEDGEMENT REQUESTS AND OTHER CONSIDERATIONS**

In general, the IRB will conduct an administrative review and acknowledge events and documents that do not require review by the IRB. Examples of such activities may include:

- External reportable events (e.g., SAEs that occur at external sites)
- Letters from sponsors
- Administrative corrections
- Publications and presentations

In general, acknowledgement requests and other considerations will be reviewed by an expedited reviewer; however, any clinical event must be reviewed by an IRB Member who is a Clinician. The reviewer may consult with other IRB Members when conducting the review or defer the review to the full board at any time.

**ADMINISTRATIVE CORRECTIONS**

Contact the IRB to request a minor administrative correction, such as a typo, or incorrect date on an IRB approved document. The change can be made by an IRB staff member who is also an IRB Member, without additional IRB approval; however, if needed, the research team may be requested to initiate the request in the electronic IRB submission and reporting system.
CONTINUING REVIEW (PROGRESS REPORTS)

IRB approval of any expedited or full board protocol is valid for a maximum of twelve (12) months from the date of the initial or prior review. The IRB may, depending on the nature of the study, require more frequent reviews by approving the protocol for periods of less than one year or requiring a progress report update after a certain number of participants are enrolled. Failure to receive continuing review and approval before the end of the current approval period will result in the expiration of IRB approval of the study.

When applicable, studies may be approved at the time of continuing review with a contingency that certain investigators cannot continue to do the research, until they submit any delinquent requirements (e.g., conflict of interest disclosures, training requirements, etc.).

For more information, see the OHRP guidance on continuing review and FDA guidance on continuing review for clinical investigations.

RESEARCH PROGRESS REPORT FORM

The IRB must receive a fully completed and signed “Research Progress Report Form” and all required materials in sufficient time to permit continuing review and approval.

If a study must be reviewed at the convened IRB, the progress report and all required materials must be provided and all required training and conflict of interest disclosures must be complete at least three (3) weeks in advance of the scheduled meeting for which the study will be reviewed. If the continuing review is eligible to be expedited, the progress report and all required materials must be provided and all required training and conflict of interest disclosures must be complete at least three (3) weeks in advance of the expiration date.

Conditional approval may possibly be granted by the IRB, when the submission is incomplete and cannot otherwise receive full approval by the expiration date; otherwise study’s IRB approval automatically expires.

If COI and CITI documents are not updated or completed in a timely manner, the IRB may close the study or modify the study to remove delinquent investigators or key personnel from the study.

Submission instructions are included within the “Application for Progress Report.”

If the continuing review study is eligible for expedited review, it will be reviewed by the IRB Chair or an experienced IRB Member; otherwise it will be reviewed by the convened (full) IRB. The reviewer may consult with other IRB Members when doing the review or defer the review to the Full Board at any time.
If the continuing review report is reviewed and approved by the IRB within thirty (30) days prior to the expiration of the study, the IRB may maintain the fixed anniversary date for the expiration of the annual approval.

**LAPSE IN CONTINUING REVIEW/EXPIRED IRB APPROVAL**

**WARNING:**
The electronic IRB submission and reporting system notifies the study team 60 days prior to the expiration of IRB approval. The PI must ensure a progress report is submitted in time for continuing review.

If a study expires before the IRB can review and approve the continuing review, the study team will get an automatic notice from the electronic IRB submission and reporting system stating the study has expired and all research must stop.

The PI must plan ahead to ensure that continuing review and re-approval of research occurs prior to the end of the approval period specified by the IRB. Procedures must be followed by PI such that lapses of IRB approval will be a rare occurrence. The Federal regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. A lapse in IRB approval of research occurs whenever a PI has failed to provide continuing review information to the IRB or the IRB has not conducted continuing review and re-approved the research by the expiration date of IRB approval.

In such circumstances, all human research activities must stop; however, the PI is still obligated to fulfill reporting requirements. Enrollment of new research participants cannot occur after the expiration of IRB approval. All human research activity must cease on the expiration date including any interactions or interventions with participants, any analysis of individually identifiable private data, and any use or disclosure of protected healthcare information (PHI) for research purposes.

Persistent failure to complete timely reports may represent continuing non-compliance of a PI, if determined as such by the IRB. If neither “Research Progress Report Form” nor a “Research Closure Report Form” is received, future studies presented to the IRB from the PI may be held until all pending reports and supporting materials are reviewed by the IRB.

**EXPIRATIONS IMPACTING THE SAFETY, RIGHTS, OR WELFARE OF ANY RESEARCH PARTICIPANTS**

If a study’s expiration impacts the safety, rights, or welfare of any participants, the PI must contact the IRB immediately. When it is in the best interest of the research participants to continue the interventions of a clinical trial that has a lapsed IRB approval, the IRB may approve
the continuation of the study but limit the activities to interventions with the research participants, until the remainder of the study can be reviewed and approved.

Temporarily continuing participation of already enrolled research participants in a research project during the period when IRB approval has lapsed may be necessary or appropriate, for example, when the research interventions hold out the prospect of direct benefit to the research participants (e.g., investigational chemotherapy regimen in an oncology trial), or when withholding those interventions poses increased risk to the research participants.

If the IRB decides that already enrolled research participants should continue to receive the interventions that were being administered under the research protocol, data collection (especially safety information) should also continue for such research participants (e.g., implantable device requiring long-term follow-up).

If the PI is initially determining whether it is in the best interests of already enrolled research participants to continue to participate in the research after IRB approval has expired, the PI should consult the treating physician (if the PI is not the treating physician). This determination may be made for all enrolled research participants as a group or for an individual research participant. In all cases, the PI should verify that the IRB Chair, Vice-Chair, or designate agrees with this determination as soon as possible. The IRB Chair or Vice-Chair will document the determination in writing and within the electronic IRB submission and reporting system, and request the IRB staff to issue a letter which will address whether the PI’s determination applies to one or more individuals and stipulate any other application information, such as time frame for which the participants may continue in the research.

RE-ACTIVATION OF EXPIRED OR CLOSED STUDIES

When IRB approval of an ongoing study lapses and the IRB subsequently re-approves (reactivates) the research, the IRB may approve the study for one year and establish a new anniversary date for the expiration date of subsequent approval periods. The IRB may also re-approve the research for a period of less than 1 year, either to retain the original anniversary date on which prior approval periods expired or to address study risks.

STUDY CLOSURE (FINAL REPORT)

In order to close a study, submit a “Final Report” Form before the deadline for continuing review. Instructions for completed the form can be found within the form. In general, a study closure report is reviewed by the IRB Chair or designated reviewer; however, it may be deferred to convened (full) IRB.
Analysis of identifiable data and the enrollment of new research participants in a protocol for which IRB approval has closed or is expired are not permitted; however, the PI is still obligated to fulfill reporting requirements.

If a PI plans to leave the DMC and does not transfer the study to another PI, the PI MUST close the study before the PI departs.

The use, storage, de-identification, retention, and/or destruction of data and specimens involved in the study must be consistent with the IRB approved protocol, DMC policy, Federal requirements, and ALL relevant applicable IRB approved documents such as the informed consent document, information sheet, HIPAA research authorization, HIPAA waiver, and sponsor requirements.

Please provide IRB with copies of presentations or publications at the time of study closure. If presentations or presentations are available after the study closure, they may be reported to the IRB for acknowledgement.

Obtain approvals to transfer research records or materials to another institution (e.g., Materials Transfer Agreement), when required.

If a funded study or a study that involves a contract is anticipated to close prematurely, the PI must immediately report this to Pre- and Post-Award.

Before a PI prematurely closes a study, (s)he and the IRB must consider whether any additional procedures need to be followed to protect the rights and welfare of current participants.

In general, study closures will be reviewed by an expedited reviewer or an experienced IRB Member; however, any clinical event must be reviewed by an IRB Member who is a clinician. The reviewer may consult with other IRB Members when conducting doing the review or defer the review to the full board at any time. Premature study closures should be reviewed by the full IRB.

REQUEST TO RE-ACTIVATE (RE-OPEN) A STUDY

An expired or closed study may be re-opened by submitting a Progress Report Form and a cover letter indicating why the study expired or closed prematurely and any applicable measures to prevent re-occurrence. Research activities cannot start until the IRB provides approval of the study re-opening through an IRB approval letter. If the study is eligible for expedited review, it may follow the expedited review process. If it is not eligible for expedited review, it will follow the review process by the full IRB.

NON-COMPLIANCE IN HUMAN RESEARCH
REPORTING POSSIBLE RESEARCH NON-COMPLIANCE TO THE IRB

Investigators and other research staff are required to report all suspected noncompliance to the IRB. A PI may voluntarily decide to suspend or terminate some or all of the research activities that may be under current review or investigation and inform the IRB of this action.

Occurrences of noncompliance may come to the attention of the IRB through other sources, including new applications, continuing reviews/progress reports, internal audits, study monitoring, adverse event reporting, reports from Data Safety Monitoring Boards, or reports from collaborators, employees, staff, research participants, patients, family members, IRB Members or others.

Research noncompliance may often be due to faulty communication or systematic error rather than the negligent actions of a single individual. Identification and investigation of noncompliance provides an opportunity for the improvement of faulty communication paths and systems, while honoring the respect of those who participate in human research. It is to this end that individuals are encouraged to identify and report suspected occurrences of research noncompliance.

REPORTING ALLEGATIONS OF NON-COMPLIANCE TO THE IRB OR OTHERS

Any allegation of non-compliance can be reported to the IRB, Office of Compliance and Audit Services (OCAS), or Institutional Official (IO). An allegation may be reported anonymously to the confidential Compliance Line (877-349-SUNY or via Compliance Line Website); however, anonymous reports must provide sufficient information to conduct an investigation, as the IRB or other officials may not be able to re-contact an anonymous resource.

Allegations of research misconduct, privacy violations, or security violations will be referred to the appropriate departments for further investigation.

All allegations of non-compliance are taken seriously. In the unlikely event that a PI is not willing to report an incident that requires reporting to the IRB, a study team member or anyone else, including a research participant, can report it to the IRB. The IRB may require additional actions or sanctions for a PI who was not willing to report the incident.

No one may retaliate against anyone making a report.

If an individual is uncomfortable with reporting apparent non-compliance through the above mechanisms, allegations of non-compliance or complaints may be made directly to the appropriate regulatory authority, such as the HHS Office for Human Research Protections, FDA, or Office of Civil Rights.
REVIEW OF POSSIBLE RESEARCH NON-COMPLIANCE

Any possible serious or continuing non-compliance must be promptly reported by the IRB to the Institutional Official (IO), and OCAS.

The IRB Chair or Vice-Chair may do any of the following:
- Take interim action as needed to eliminate apparent immediate hazards or protect the well-being of research participants;
- Determine whether the concern is non-compliance;
- Determine whether non-compliance is not-serious and not continuing; or
- Determine whether non-compliance appears to be serious or continuing and as such, defer the review to the convened IRB and promptly notify the IO.

Only a convened IRB is authorized to make a determination of serious non-compliance or continuing non-compliance. The convened IRB must review any apparent serious or continuing non-compliance that appears to be serious or continuing, at the earliest practicable opportunity.

The IRB must determine and document whether or not any non-compliance that may appear to be serious or continuing non-compliance actually occurred. In reviewing information to make a final determination of serious or continuing non-compliance, the convened IRB may consider:
- Whether any additional information is required;
- Whether an audit report and any other available information sufficiently supports a determination of non-compliance;
- Whether an audit report and any other available information supports the need to suspend or terminate the research in order to protect research participants or others;
- Additional actions to protect the rights and welfare of currently enrolled participants;
- Whether procedures for withdrawal of enrolled participants account for their rights and welfare; or
- Whether participants should be informed of the noncompliance and/or any of the corrective actions.

In considering actions for serious or continuing non-compliance, the IRB seeks to:
- Correct the non-compliance,
- Deter it from occurring again (e.g., hold the relevant individuals accountable for their actions and provide education on how to comply), and
- Attempt to mitigate any adverse effects on participants.

If the IRB determines that serious or continuing noncompliance occurred, the IRB must document the IRB determination and determine if remedial actions are needed to ensure present and/or future compliance, which may include, but not limited to, any of the following:
- Convene an investigation committee
- Conduct or request a for-cause audit
- Require follow-up audit(s)
- Suspension or termination of the study procedures/enrollment or IRB approval.
- Suspension of other projects conducted by the same investigator
- Notification of current research participants (required when such information may relate to participants’ willingness to continue to take part in the research)
- Modification of the study protocol or informed consent document
• Require current research participants are re-consented to continue participation
• Require monitoring of the research
• Modification of the continuing review schedule
• Require observation of consent procedures
• Require more frequent review of the conduct of the research
• Require additional training for the research team
• Refer issues to other institutional entities (e.g., Institutional Official, applicable Dean, applicable Department Chairs, Legal Counsel, Risk Management, Privacy Officer, Data Security Officer, Performance Improvement, etc.)
• Imposition of restrictions as a condition for the continuation of research
• Destruction of data collected during the period of Noncompliance;
• Disallowance of the publication of data collected during the period of Noncompliance;
• Additional oversight monitoring
• Any other action deemed appropriate by the IRB to protect the rights and welfare of research participants
• When appropriate, applying any corrective action to all similar protocols.

Written notice of the IRB determination will be provided for the investigator, including the time frame for which corrective actions are required.

If apparent serious or continuing noncompliance was identified by an audit or through an allegation of non-compliance, the IRB should notify the auditor or the complainant within 15 business days after its final determinations have been provided to the PI, regardless of outcome.

The IRB must promptly notify the IO after making determinations of serious or continuing non-compliance. The IO may notify the appropriate Dean and/or Department Chair of the PI's Department. Any other necessary investigations or reporting to federal agencies or sponsors will be completed or directed by the IO.

The PI must initiate the corrective actions within the required deadline of the IRB and notify the IRB when the actions are complete. The deadline determined by the IRB should be no greater than 120 calendar days after any determination of noncompliance, except where remediation requires substantial renovation or fiscal expenditure, hiring, legal negotiations, or other extenuating circumstances. A failure to implement the corrective plan on time may require further action, including suspension or termination of IRB approval of the research protocol. Where remedial actions cannot be completed within the required deadline, the PI must notify the IRB, Department Chair, appropriate Dean, and IO of the delay.

If the IRB action will affect participants in the protocol (e.g., requires withdrawal of participants), the IRB shall utilize a process that takes into account the impact on the health and safety of the research participants.

If anyone has concerns related to the integrity or objectivity of any aspect of an IRB determination or an investigation, (s)he should discuss such concerns with the IO.
The IRB, the IO, or OCAS may determine that an additional investigation is warranted and whether the investigation should be expanded beyond the specific allegation or IRB determination (e.g., research misconduct). If any facts are at issue, the IRB, IO, or OCAS may contact any appropriate persons for verification of such facts.

The IRB, or an Investigation Committee appointed by the IRB, IO, or OCAS, may invite the PI or other research staff to a portion of the meeting to answer questions and to discuss the issue of noncompliance. The PI or other research staff may be accompanied by a faculty representative, legal counsel, union representative, or another member of his or her department. The role of these individuals is limited to providing information and support to the PI; however, they will not participate in the discussion between the PI and the IRB or Investigation Committee.

### Appealing DMC IRB Decisions

The IRB functions independently when granting approval and disapproval of research. Research covered by this policy that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve human research that has not been approved by the IRB.

A PI may appeal any IRB decision, with the exception of the IRB decisions to suspend or terminate IRB approval of research.

To appeal, the PI must submit a written appeal to the IRB Chair via the electronic IRB submission and reporting system that address or appeal the IRB’s concerns, within 60 days of receiving the written notice of disapproval, deferral, or decision. If the Chair does not agree with the appeal, the Chair will defer it to the Full IRB.

In cases where there is disagreement between any IRB action and the PI regarding the IRB decision or 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 Institutional Official may organize a meeting to help facilitate discussion between the IRB and the PI. While the Institutional Official may provide input and make recommendations to the IRB for expeditious resolution of the matter, final recommendations for approval remain under the purview of a convened (full) board meeting, which will make the final decision.

### Reporting and Investigation of Allegations of Undue Influence

If the IRB Chair, a member, or representative from the IRB's administrative staff feels that the IRB Committee has been unduly influenced by any party, they shall make a confidential communication to the Institutional Official or Vice President for research, or via confidential Compliance Line (877-349-SUNY or via Compliance Line Website) depending on the circumstances. The official receiving the confidential communication will conduct a thorough investigation and applicable corrective action will be taken to prevent additional occurrences.
REFERENCES

- AAHRP Standards
- AAHRP Tip Sheet 24: Relying on an External IRB
- AAHRPP Accreditation Standards
- Clinical Trials Transformation Initiative
- DMC Office of Compliance and Audit Services HIPAA Policy
- DMC Policy AD-1, Guidelines for Preparation Format, Review, Distribution and Retention of Hospital Policy
- DMC Policy HIPAA-28: Uses and Disclosures for research Purposes
- DMC HIPPA-32 policy: Uses and Disclosures Requiring Patient Authorization
- DMC’s Investigational Drug Dispensing and Utilization Policy (PHA-11)
- FAQs - Clinical Studies Involving Electronic Cigarettes and INDs
- FDA 21 CFR 50.24: Exception from Informed Consent (EFIC) Requirements for Emergency research
- FDA Amendments Act of 2007 (FDAAA)
- FDA Draft Guidance on IDNs – Determining Whether Human research Studies Can Be Conducted Without an IND
- FDA FAQs for Form 1572.
- FDA Guidance for Clinical Investigators, Sponsors, and IRBs: AE Reporting to IRBs- Improving Research Participants Protections (January 2009)
- FDA Guidance for Industry Using a Centralized IRB Review Process in Multicenter Clinical Trials
- FDA Guidance for informed consent.
- FDA Guidance for Investigator Responsibilities
- FDA Guidance on Exception from Informed Consent Requirements for Emergency research
- FDA Guidance on IRB Continuing Review after Clinical Investigation Approval
- FDA Guidance on Marijuana research with Human Subjects
- FDA guidance on SR and NSR Medical Device Studies
- FDA ICH Guidance Documents
- FDA Investigator Responsibilities for Investigator-Initiated IND Applications
- FDA Investigator’s Responsibilities for INDs
- FDA Recruiting Study Subjects- Information Sheet
- FDA regulations (21 CFR 50, 56, 312, 812) for clinical trials and device studies
• FDA website on IDE Responsibilities
• FDA Website: Protection of Human Subjects; Informed Consent and Waiver of Informed Consent Requirements in Certain Emergency research
• FDA’s Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors: Significant Risk and Nonsignificant Risk Medical Device Studies
• Federal Privacy Act
• Health Information Privacy: research
• HHS 42 CFR Part 50, Subpart F – Promoting Objectivity in research
• HHS 42 CFR Part 50; HHS 42 CFR Part 94 - Responsibility of Applicants for Promoting Objectivity in research for which Public Health Service Funding is Sought and Responsible Prospective Contractors
• HHS 45 CFR 2 –Confidentiality of Alcohol and Drug Abuse Patient Records
• HHS 45 CFR 46 (Revised January 15, 2009, Effective July 14, 2009)
• HHS 45 CFR 46 (Revised January 19, 2017, Effective January 19, 2018)
• HHS Health Information Privacy Website
• HHS Office for Civil Rights (OCR) Health Insurance Portability and Accountability Act of 1996 (HIPAA) or 45 CFR Parts 160, 162, and 164
• Medicare Clinical Trial Policies
• National Cancer Institute Central IRB
• New York Codes, Rules and Regulations, Title 14, Department of Mental Hygiene, Part 527, Rights of Patients
• New York Mental Hygiene Law, Article 81
• New York State’s Public Health Law 18: Access to Patient Records
• New York’s Family Health Care Decisions Act (FHCDA) (Public Health Law §29-CC)
• NIH Guidance: Protecting PHI in research: Understanding the HIPAA Privacy Rule
• NY State Department of Health HIPPA Preemption Charts
• NYS 10 NYCRR Part 63 (HIV/AIDS Testing, Reporting and Confidentiality of HIV-Related Information
• NYS 1-2.13 NY Estates Powers and Trusts Law
• NYS Civil Rights Law Section 79-L (Confidentiality of genetic tests)
• NYS DOH HIPAA Preemption Charts
• OCR Health Information Technology for Economic and Clinical Health (HITECH) Act, enacted as part of the American Recovery and Reinvestment Act of 2009
• Office of Human research Protections’ Guidance “Obtaining and Documenting Informed Consent of Research Participants Who Do Not Speak English”
• OHRP guidance on Approval of research with Conditions
• OHRP Guidance: FAQs
• OHRP Guidance: Informed Consent Requirements in Emergency research, for research not subject to FDA regulations
• OHRP Guidance: IRB Review of Clinical Trial Websites
• OHRP Guidance: Use of a Central IRB
• OHRP International Program website
• U.S. Department of Education, Title 34 Part 350: Disability and Rehabilitation Projects and Centers Program
• U.S. Department of Education, Title 34 Part 356: Disability and Rehabilitation research
• U.S. Department of Health and Human Services (HHS) Regulations for Protection of Research Participants under 45 CFR 46 (including Subparts A, B, C, D, and E)
• U.S. Food and Drug Administration (FDA) regulations under 21 CFR 11, 50, 56, 312, 812, and 814
### REVIEW HISTORY

**Supersedes:**

2004 Investigators Manual
- John M. Allen
- Enzo Bard

2015 IRB Policies and Procedures Manual (Draft)
- IRB Steering Committee
- Rebecca S. Twersky MD, MPH
- Richard Coico, MS, Ph.D.
- Shoshana Milstein, RHIA, CHP, CCS
- Phyllis Supino, EdD
- Stanley Friedman, MD
- Kathleen Powderly, Ph.D.
- Nicole McNair, MS
- Diann Johnson, MPH
- F. Lisa Murtha, Esq.

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