

Einstein IRB Member Handbook

Office of Human Research Affairs
Albert Einstein College of Medicine
and
Montefiore Medical Center¹

¹ This handbook has been adapted from the University of Southern California Office for the Protection of Research Subjects Community Member Resource Manual.

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This manual is a useful training tool and a reference designed to improve the IRB member experience.

Once comfortable with this information, it is recommended that the readers of this guide explore the following websites:

Office of Human Research Affairs:

<https://einsteinmed.edu/administration/human-research-affairs/>

Federal Office for Human Research Protections:

<http://www.hhs.gov/ohrp/>

Food and Drug Administration:

<http://www.fda.gov/>

These websites provide extensive resources and information on human subjects protections.

CHAPTER 1: Introduction to the HRPP and IRB

This chapter provides basic information for those interested in serving as a member on an IRB and is designed to answer common questions. It also provides a brief history of the development of regulations governing human subjects research.

Defining Human Subjects Research

Federal regulations charge IRBs with the responsibility of reviewing human subjects research. Any studies that meets the definition of “human subjects research” falls under the purview of the IRB. Federal regulations define “human subject” and “research” in a way that differs from common use of those terms.

The following are the federal definitions (45 CFR 46, also known as the “Common Rule”):

Research is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

A **human subject** is a living individual **about** whom an investigator (whether professional or student) conducting research (1) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (2) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

The Human Subjects Protection Program (HRPP)

Albert Einstein College of Medicine (Einstein) and Montefiore Medical Center (MMC) operate a Human Research Protection Program (HRPP) to review and approve all human subjects research at affiliated institutions. The HRPP encompasses many levels of administration and academic programs. Protection of human subjects in research is a shared responsibility among various components of a research institution. The IRB, the most visible part of the HRPP, is but one component. Legal offices, oversight offices, institutional administration, researchers, and even research volunteers also share this responsibility and all play an important role in the program’s success.

The Office of Human Research Affairs (OHRA) oversees human subjects’ protections through program oversight, education, policy setting, and outreach. The Einstein IRB is empowered to review all human subjects research proposals which are conducted by affiliated faculty, staff, or students. The researchers and participants are expected to honor the terms under which they have agreed to participate in the research process.

The Institutional Review Board (IRB)

The IRB is an oversight committee charged with reviewing all research involving human subjects to ensure research complies with institutional policies and state, local, and federal laws. The IRB has the authority to approve, require changes to the study procedures, or disapprove proposed research projects.

The IRB functions as a surrogate “human subject advocate.” Its role is to safeguard the rights and welfare of research subjects by evaluating the research to assure an acceptable balance of risks to benefits. Under the terms of the Common Rule, the IRB must:

- Have at least five members
- Include individuals from academic disciplines relevant to the research being reviewed Include at least one non-affiliated member
- Be diverse in terms of race, gender and cultural background.
- Have the necessary experience and expertise to fairly evaluate the proposed research.

IRB members can be faculty, staff, or students from the institution, and members from the local community.

Brief History of Human Subjects Research Regulations

The modern history of ethical standards for human subjects research began in the 1940s with the Nuremberg Code. Since then, the U.S. federal government has increased awareness for protecting the rights and welfare of human subjects by establishing regulatory codes and regulations. This section provides a brief background on the history of the regulations and ethics that are required when human subjects are involved in research.

Nuremberg Code

The Nuremberg Code was developed following the Nuremberg Military Tribunal which judged Nazi doctors conducting human experimentation. The Code encompasses many of the basic principles governing the ethical conduct of human subjects research today. The Nuremberg Code states that “the voluntary consent of the human subject is absolutely essential” and it further explains the details implied by this requirement: capacity of participants to consent, participants’ rights to participate or not, freedom from coercion, no penalty for withdrawal, and comprehension of the risks and benefits involved.

Declaration of Helsinki

In 1964, the World Medical Association established recommendations to guide medical doctors in biomedical research involving human subjects. The Declaration governs international research ethics and defines rules for "research combined with clinical care" and "non-therapeutic research." The Declaration of Helsinki was revised in 1975, 1983, 1989, 1996, 2000, and 2008 and is the basis for Good Clinical Practices used today.

Issues addressed in the Declaration of Helsinki include:

- Research involving medical interventions with humans should be based on the results from laboratory and animal experimentation.
- Research protocols should be reviewed by an independent committee prior to initiation.
- Informed consent from research participants is necessary.
- Research should be conducted by medically/scientifically qualified individuals.
- Risks should not exceed benefits.

Belmont Report

In 1979, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research wrote “The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research.” The Belmont Report sets forth the basic three ethical principles expected to be followed when doing research involving human subjects: respect for persons (autonomy), beneficence, and justice.

- **Respect for Persons:** “Respect for persons incorporates at least two ethical convictions: first, individuals should be treated as autonomous agents, and second, persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.”

In short, this states that the person must be capable of making the decision on whether or not to participate in a human subjects research project.

- **Beneficence:** “Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In [the Belmont Report], beneficence is understood in a stronger sense, as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense:
 - (1) do not harm; and
 - (2) maximize possible benefits and minimize possible harms”
- **Justice:** “Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property on the basis of which burdens and benefits should be distributed. These formulations are:
 - (1) to each person an equal share,
 - (2) to each person according to individual need,
 - (3) to each person according to individual effort,
 - (4) to each person according to societal contribution, and
 - (5) to each person according to merit.”

Federal Policy for the Protection of Human Subjects (Common Rule)

In 1981, the Department of Health and Human Services codified the Policy for the Protection of Human Subjects (Title 45, Part 46). These regulations, called the “Common Rule,” provide for the basic foundation of Institutional Review Boards. This Federal Policy has been codified by the 18 federal agencies that conduct, support, or otherwise regulate human subjects research, hence the title “Common Rule.” The Policy also provides additional protections to specific populations, such as pregnant women, fetuses, and neonates (Subpart B), prisoners (Subpart C), and children (Subpart D) involved in human subjects research.

In January 2019, a revised Common Rule went into effect.

United States Food and Drug Administration Regulations

The U.S. Food and Drug Administration, within the Department of Health and Human Services, regulates drugs, medical devices, and biologics. FDA regulations 21 CFR Part 50 (Protection of Human Subjects), and 21 CFR Part 56 (Institutional Review Boards) must be adhered to when studies are conducted using drugs, medical devices, or biologics. Although FDA regulations are similar to the regulations found in the Common Rule, there are some differences.

Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule

The Health Insurance Portability and Accountability Act Privacy Rule (HIPAA) is a federal law that generally prohibits health care providers (such as physicians or other health care practitioners, hospitals, nursing

facilities and clinics) from using or disclosing "protected health information" (PHI) without written authorization from the patient.

If an investigator intends to create, use, or release to others (e.g., sponsors, other investigators, collaborators) any identifiable health information in connection with their research, he/she must indicate that in the IRB application.

When reviewing proposed research, the IRB serves as the Privacy Board and can approve waivers or alterations of HIPAA authorization for use of PHI.

Protected Health Information (PHI) is health information transmitted or maintained in any form or medium that includes ALL of the three following parts:

- identifies or could be used to identify an individual; and
- is created or received by a healthcare provider, health plan, or healthcare clearinghouse; and
- relates to the past, present, or future physical or mental health or condition of an individual; the provision of healthcare to an individual; or the past, present, or future payment for the provision of healthcare to an individual.

The full text of the updated HIPAA Privacy Rule can be found at the Office for Civil Rights (OCR) website: <http://www.hhs.gov/ocr/privacy/hipaa/administrative/privacyrule/index.html>.

Chapter 2: IRB 101

What is expected of an IRB Member?

A considerable time commitment is required when serving as an IRB member. IRB members need to set aside blocks of time to review IRB applications and protocols, attend meetings, and avail themselves to educational opportunities. The amount of time needed will gradually lessen as the process becomes familiar. Keep in mind - some studies are so technical, complex, and dense, that other IRB members or consultants will need to review the most technical sections in addition to your review.

IRB Members are expected to:

Upon appointment to the Einstein IRB

- Submit a resume or CV to the IRB office.
- Satisfy training and education requirements for IRB Members

Upon completion of the above

- Review and critique research applications.
- Review all submissions on the meeting agenda.
- Review expedited minutes linked to the agenda, and if issues or errors are found resolve them with the IRB staff.
- Assure that applications include adequate protections for human subjects in the research plan.
- When assigned as a reviewer, post the review in the electronic IRB system (iRIS) at least two days prior to the meeting.
- Send the completed reviewer's checklist to the analyst processing the submission.
- Voice issues—either publicly or privately—that are noted while reviewing the protocol, including “gut feelings” that can't be adequately defined.
- Attend IRB meetings and education sessions
- Inform the OHRA staff of your availability to attend scheduled meetings, and notify ORHA staff immediately if you are unable to attend a meeting to which you had previously committed.
- Possess basic computer, internet, and word processing skills to review protocols and communicate with the IRB staff/members and investigators.
- Absent yourself from discussion and voting on any project where there is a potential or real conflict of interest.
- Maintain confidentiality for all discussions, reviews, meeting minutes, and proprietary information you will encounter as an IRB member.
- Return any IRB-related documents to IRB staff at the end of the meeting, and shred any documents you may have printed for review at your home or office.

IRB Policies and Procedures

IRBs are expected to follow federal, state, and local laws, as well as regulatory and institutional policies. In addition to these requirements, IRBs examine ethical issues when reviewing research projects. For the Einstein IRB, a comprehensive set of policies and procedures can be found at the following address:

<https://einsteinmed.edu/administration/human-research-affairs/>

IRB members should familiarize themselves with these policies and procedures and refer to them when completing reviews.

IRB Staff

IRB staff are employed by the institution and comprise the IRB office. Their duties include preparing agendas, conducting initial regulatory screening of protocols, compiling correspondence, taking minutes, providing support for investigators and researchers, and arranging IRB meetings. Each study or protocol that is submitted for IRB review is assigned to a staff reviewer to begin the process. This person is responsible for screening the protocol and solving as many issues as possible before the study is reviewed by an IRB member. These may include obtaining missing documents, getting answers to regulatory and administrative questions, or addressing problems that will delay IRB approval.

Staff members know a great deal about the regulations governing research. IRB staff often have backgrounds in research, including research administration, clinical research, the medical and legal fields, and the social sciences. They come to the process with a strong knowledge of the regulations, and the institutional culture. As a result, they are a great help to community members, IRB reviewers, and the research team—and a wonderful resource to call on if you have questions or want help.

Regulatory Levels of IRB Review

The “Common Rule” (45 CFR 46) provides for three levels of review for human subjects research. They are exempt, expedited, and full board.²

Exempt Review: Exempt research involves research with human subjects, but because of its nature and “minimal risk” it is “exempt” from the provisions of the Code of Federal Regulations. Exempt research projects must still be submitted to the IRB for initial review. Changes to exempt research must be submitted to the IRB for review and approval only if the project is amended in such a way that it no longer meets the exemption criteria, or if there is a change in PI.

An IRB member or designated staff determines if a research project falls under one or more of the following eight exempt categories listed in the federal regulations (45 CFR 46.104):

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

² Note that not all research using human subjects require IRB review. Studies that do not meet the regulatory definitions of “human subject” or “research” are relegated to a category the Einstein IRB calls Not Human Subjects Research (NHSR).

- and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
2. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:
 - a. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
 - b. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
 - c. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review of the privacy and confidentiality measures.³
 3. Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:
 - a. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
 - b. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
 - c. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review of the privacy and confidentiality measures.
 - i. For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.
 - ii. If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

³ Note, categories 2-a and 2-b can only be applied to studies involving children if the PI plans only to observe and not interact with children. Category 2-c cannot be applied to any research involving children.

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:
 - a. The identifiable private information or identifiable biospecimens are publicly available;
 - b. Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;
 - c. Collection and analysis involving investigators use of identifiable health information when use is regulated by HIPAA “health care operations” or “research” or “public health activities and purposes”⁴; or
 - d. Research information collected by or on behalf of federal government using government generated or collected information obtained for non-research activities.
5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants.
6. Taste and food quality evaluation and consumer acceptance studies.
7. Storage or maintenance of identifiable private information or identifiable biospecimens for secondary research for which broad consent is required.⁵
8. Secondary research involving use of identifiable private information or identifiable biospecimens for which broad consent was required.⁶

Expedited Review: If the level of risk in a research project is considered to be no greater than minimal, and the research meets at least one of the expedited categories below, the IRB may review the project as expedited. Expedited review covers the same considerations as a full committee review. However, the project can be reviewed and approved by the IRB Chair or one Designated Reviewer, rather than the whole convened IRB committee. In reviewing research, expedited reviewers may exercise all of the authorities of the IRB, except the reviewer may not disapprove the research. In this case, the expedited reviewer must defer review to the full IRB committee. There are nine expedited categories listed in the federal regulations (45 CFR 46.110):

The federally defined expedited categories are:

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

⁴ Note that Albert Einstein College of Medicine is not a HIPAA-covered entity. Therefore, the Einstein IRB does not make use of this category, since we cannot track when research data is or is not protected by HIPAA laws.

⁵ The Einstein IRB will not be implementing this category due to the impracticability of implementing “broad consent,” or an open-ended permission to use identifiable private information or biospecimens for unspecified future research. To implement broad consent, we would have to track all refusals, which would be a serious logistical challenge.

⁶ The Einstein IRB will not be implementing this category due to the logistical challenges of implementing broad consent.

- a. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
- b. Research on medical devices for which (i) an investigational device exemption application (21 CFR 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
 - a. from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
 - b. from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
3. Prospective collection of biological specimens for research purposes by noninvasive means.
 - a. Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.
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).
 - a. Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. This listing refers only to research that is not exempt.)
6. Collection of data from voice, video, digital, or image recordings made for research purposes.

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

There are two additional categories, but they apply only to continuing review of research that has already been approved:

8. Continuing review of research previously approved by the convened IRB as follows:
 - a. where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
 - b. where no subjects have been enrolled and no additional risks have been identified; or
 - c. where the remaining research activities are limited to data analysis.
9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Full Board Review: Studies that involve more than minimal risk require full board review at a convened meeting, at which a quorum of IRB members is present, including a community member. For the research to be approved, it must receive the approval of a majority of those members present. While federal regulations do not specifically list categories that would fall under full board review, below are certain criteria that may require full board review.

1. Clinical procedures involving drugs, devices, or biologics;
2. Studies using vulnerable populations;
3. Drug, device, or biologics studies taking place internationally (particularly those countries with little or no provisions for protection of human subjects);
4. Studies where information may be disclosed to researchers that could require mandatory legal reporting (e.g., child/elder abuse, drugs, etc.);
5. Studies involving deception which raise the risk level;
6. Studies where the IRB staff, chair, member, or designee, determines to be greater than minimal risk.

Single IRB studies

The basis for the single IRB model is to allow multiple sites that are conducting the same protocol to use a single IRB for review, instead of using multiple IRBs to review the research at the sites individually. The single IRB model has been in use for many years, across a wide variety of studies and circumstances. Due to recent regulatory changes at the National Institutes of Health (NIH) and Office of Human Research Protections (OHRP), the single IRB model has become more prevalent

Decisions about whether Einstein will enter into a reliance agreement for IRB review, whereby the Albert Einstein College of Medicine & Montefiore Medical Center will provide IRB review for other institutions (“Reviewing IRB”) or will rely on the IRB at another institution (“Relying Institution”), require consideration of

specific information about the proposed research and the institutions that are involved via submission of an [IRB Reliance Request Form](#). Reliance can be for a single study or series of studies, and the reviewing IRB in a reliance relationship can be referred to as a Reviewing IRB, a Single IRB or a Central IRB. The IRB that will be responsible for IRB review in all such reliance relationships will be referred to as a "**Reviewing IRB**".

Reliance cannot begin until a reliance agreement has been reviewed and fully executed. The Einstein IRB Office will facilitate this process via iRIS.

Details on what is required in iRIS following execution of a reliance agreement are detailed in the [sIRB Reliance Procedure SOP](#).

Definitions

Reliance Agreement: An arrangement between institutions allowing one institution to rely on the IRB of another institution for review of human subjects research.

Relying Site (RS): The site that relies on another organization's IRB for review of human subjects research.

Reviewing IRB: The IRB that assumes IRB responsibilities for another organization. When multiple institutions conduct the same study and one IRB will conduct the review for all study sites, the Reviewing IRB may be called a Single or Central IRB (collectively, "sIRB").

Common Types of IRB Submissions

New Protocols: Initial review of research submissions

Progress Report: yearly review required for full board projects

Amendment: any change in risk, personnel, scope, procedures, etc.

Reportable Event: adverse events and unanticipated problems involving risks to subjects or others, protocol deviations, or noncompliance

Protocol Registrations: studies ceded out to external IRBs following execution of applicable reliance agreements

Conflicts of Interest

The term "conflict of interest" (COI) refers to situations in which financial or other personal considerations compromise, or have the potential to compromise, an individual's professional judgment or objectivity. Conflict of interest may occur with the researcher, IRB member, or the institution. All three types of COI must be reviewed and managed by the institution or its designated committee.

Researcher COI may occur in proposing, conducting or reporting research. The bias caused by such conflicts may affect collection, analysis, and interpretation of data, hiring of staff, procurement of materials, sharing of results, choice of protocol, involvement of human subjects, and the use of statistical methods. Federal funding requires researchers to annually disclose financial interests such as consultation fees or sponsored travel that could influence their research.

Institutional COI is a growing issue that is increasingly being noted by institutions and regulatory bodies. Finding those projects where the institution has interests that may conflict with the research outcome is of special concern in human subjects research. Institutional COI is a difficult issue to identify and resolve because of the variety of ways an institution can be an “interested stakeholder” or have other interest in the conduct or outcome of a project.

IRB Members who have an “outside” interest or relationship to a research project or investigator are prohibited from participating in the vote and discussion of the project. IRB members are both required to recuse themselves (leave the meeting room) before the discussion and prohibited from voting on a study in which they have a COI. In some cases, the IRB may request a member to be present in order to provide information to the committee. Unless an IRB member declares a conflict of interest, their unbiased ability to review a project is assumed.

Disclosures of researcher conflicts of interest are reviewed by the Einstein Conflict of Interest Committee (“COIC”). The COIC will inform the Einstein IRB of any COI management plans in place for the proposed research. The IRB will review the COI management plan to determine if the specific mechanisms proposed to mitigate the conflict are adequate to protect potential research subjects. The IRB has the final authority to decide whether the interest and its management, if any, allows the research to be approved

Chapter 3: The Full Board Meeting

Full board meetings can be intellectually demanding. The credibility and integrity of the IRB review process depends upon the committee's ability to identify and address ethical issues in human subjects research. All IRB members must pay attention to written material and meeting discussions, voice their opinions when appropriate, and ask questions when they need clarification. This chapter guides an IRB member's initial experience of a full board meeting by describing the review process, defining voting options, and providing tips for reviewing a study.

Sequence of Events at Meetings

The format for discussion of protocols at the full board committee meeting is not set by federal regulations or guidance documents. Thus, IRBs are able to develop a routine that works for their institution and membership.

What follows is a basic order of Einstein IRB meetings:

1. The meeting starts with review and approval of the minutes from the previous meeting.
2. The Chair reminds members about the IRB member Conflict of Interest Policy and asks if any conflicts exist among those present.
3. The Chair or assigned IRB members present progress report submissions to update the board on the status of the studies, and votes are taken to renew their approval periods.
4. The board reviews each initial submission as follows:
 - a. The primary reviewer presents a BRIEF summary of study. The Board members should have already read the protocol, so there is no need to for the primary review to re-explain.
 - b. The primary reviewer presents ALL major problems/questions.
 - c. The secondary reviewer focuses on the consent form. The secondary reviewer does not need to repeat what was already discussed. If there are no additional issues, they may state so.
 - d. Specific minor revisions (including mention of minor consent revisions) do not need to be discussed. Reviewers can simply note that minor consent changes will be forwarded to the analyst.
 - e. Controversial issues are discussed, one by one.
 - f. The statistician reviewer provides comments.
 - g. Investigators are generally invited to participate in the discussion about their study, though they must leave before the IRB calls for a vote.
 - h. The Chair states confirms the regulatory findings (e.g., 111 approval criteria, vulnerable population criteria, IND/IDE status, HIPAA waiver).
 - i. The chair ends the discussion and calls for a vote to approve, accept with contingencies, table, or disapprove.
5. The Chair or assigned IRB members present amendments to previously-approved studies if any, and votes are taken.

An ideal environment is one that promotes an open discussion and encourages all members to express their views in a warm atmosphere, and all IRB members participate in identifying and discussing the issues. There is no formula for this process so it is essential that the IRB chair manage this aspect of the meeting. The chair determines when all of the important issues have been raised, declares the discussion over, and calls for the

vote. Questions of regulatory or policy matters are often addressed by the Chair or IRB Director as IRB members are not expected to be as expert in these areas.

Voting Options at Meetings

Approved: The study meets the regulatory criteria for IRB approval as defined by 45 CFR 46.111 and/or 21 CFR 56.111. The application has secured approval, thus the investigator is not required to make changes to the protocol or IRB application. IRB approval is valid for one year, unless the committee designates a shorter period due to higher levels of risk. An approval letter is sent to the investigator. The consent documents (if any) are stamped with the IRB approval dates. The investigator may start enrolling subjects.

Approved Pending: A study may be “approved pending” if only non-substantive changes are necessary to gain final approval. Examples of such minor non-substantive requested changes include:

- 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 ethics training);
- Directed language changes to protocol or informed consent documents; or
- Directed changes to protocol or informed consent documents along with clearly stated parameters that the changes must satisfy.

If a study is “approved pending,” the investigator’s response to the requests does not need to go back to the full board for approval. Rather, it can be done via “expedited” review.

Deferred: A study may be deferred because of substantive changes requested by the committee, or other issues related to the criteria for approval. The investigator’s response to the requested changes will come back to the full board for review.

Disapproved: A study may be disapproved if the magnitude and/or number of concerns, questions, and problems are such that an “approved pending” or “deferred” decision are inappropriate. In contrast to deferral, which implies that the study may be approvable pending substantive changes, disapproval of research should be reserved for when the board cannot reasonably imagine revising the study in such a way that the benefits outweigh the risks.

Tabled: A study may be tabled if the IRB determines that it does not have enough information to vote on a study.

Recuse: If an IRB member is listed in a study under IRB review or has any other conflict of interest, they may not participate in the initial or continuing review of the study (or an amendment) except to provide information requested by the IRB. The IRB member must leave the room (e.g. “recuse” themselves for the discussion and vote). The meeting minutes will reflect this. The chair requests IRB members with a conflict of interest to leave the room and not participate in the vote or discussion. Conflicts of interest include financial interest, active participation in the trial as principal investigator or co-investigator, or any other issue for which the member feels his or her vote could be potentially conflicted.

Abstain: If an IRB member does not have a “conflict” but is unable to vote (e.g., left the room during discussion, does not comprehend the study or the issues) the member may “abstain” from voting. A vote to “abstain” will be included as part of the voting quorum. The meeting minutes will reflect this.

Chapter 4: The Review Process

What follows is a basic overview of each stage in the IRB review process from online submission to IRB approval:

1. Principal Investigator (Faculty/Staff/Student) Designs and Submits Study via iRIS: Investigators design their protocol and submit it via the iRIS application system. Investigators must indicate if the application requires exempt, expedited, or full board review. The final determination of the review category is made by the IRB.
2. Department Chair Signoff to Ensure Adequate Proposal: Once the application is submitted (via the online iRIS application system) the department chair must review and sign off on the application. This signoff represents consideration of scientific merit, availability of resources, or other issues at the department level.
3. Verification of human subjects education: iRIS automatically verifies that basic human subjects and GCP (Good Clinical Practice) education requirements are met.
4. Conflict of Interest Review: The Conflict of Interest Committee reviews the investigators' declared conflicts of interests. If necessary, they generate a conflict of interest management plan to mitigate any potential conflicts of interest with the proposed research.
5. IRB Office: After the department chair and conflict of interest reviews have been completed, an initial review of the application is conducted by the IRB staff. IRB staff conducts a thorough pre-review of the application to verify the correct level of review, and to evaluate the protocol and supporting documents (e.g., consent form, recruitment materials, etc.).
6. IRB Review: For studies designated as expedited or full board, IRB review is required from a designated reviewer or the full board, respectively.
7. Study Approved and PI Notified: The researcher will be notified through an iRIS generated email when the study has been approved.

What Documents Should I Review?

All IRB members are expected to review the following documents for each submission on the agenda:

Initial Submissions:

- Application Form
- Protocol
- Consent Form
- Recruitment Materials

Progress Reports:

- Progress Report Form
- Application Form
- Protocol
- Consent Form
- Summary of Modifications

Amendments:

- All modified documents

If you are assigned as a primary or secondary reviewer, you should review the complete protocol file.

When Might I be Asked to Serve as a Reviewer?

The IRB Chair or Director may determine that a new member is ready to take on assigned reviewer responsibilities once they have become familiarized with the IRB review process. The following requirements and scenarios may indicate readiness to serve as a primary reviewer:

- Attended a sufficient number of IRB meetings to feel comfortable
- A sufficient knowledge of IRB policies and procedures to give a meaningful review
- Completed satisfactory reviews as a secondary reviewer
- Expertise in the area of the study
- Adequate time to prepare for the meeting and give a thorough review
- Achieved sufficient confidence to proceed with a review
- Availability when other members are unavailable, on vacation, or have a large number of items pending review
- Spoken up at a meeting with concern about the study or consent form

How to Review a Protocol

Two reviewer checklists are required to be completed for each submission. One reviewer checklist is emailed directly to the board member by the analyst. Another reviewer checklist is in iRIS. These checklists are accessible once the board member is assigned as reviewer.

Assignments for board meetings are typically done 7 to 10 days prior to the board meeting.

Using the reviewer checklist is a good way to review initial submissions (including protocols, support materials, and consent documents). Reviewer checklists have been created to help identify regulatory requirements and to note the ethical expectations that must be met.

IRB members may always call the IRB staff or another IRB member if something is unclear, missing, or prompts questions about the proper course of action.

Presenting to the IRB

Presenting Initial Submissions (New protocols)

Each initial submission should take, on average, **10 minutes**, to present and discuss. Studies for which controverted issues are raised at the meeting should take about 15 minutes to review, discuss, and vote on. Hence, *it's extremely important that issues be worked out prior to sending studies to meetings.*

Before the Meeting

- Primary and secondary reviewers should contact PIs (contact information provided on your reviewer checklist) by email to clarify issues *prior* to meetings, and should copy the IRB Chair, the other reviewer (primary or secondary), and the IRB Operations Manager.

- Reviewers may also choose to reach out to the PI by phone prior to the meeting, and should also send a quick email summary of the discussion to the Chair, the other reviewer (primary or secondary), and the IRB Operations Manager. **If your only comments are directed changes to the consent document(s), then do not send those to the PI, rather to the IRB staff only.**

At the Meeting

Reviewers should not spend meeting time asking the PI questions that can be addressed beforehand. PIs call in to or attend meetings so that they can respond to any **further** issues that arise **based on full board discussion.**

1. **1-2 minutes - Primary Reviewer** presents BRIEF summary of study. A few sentences. The Board members should have already read the protocol so there's not need to re-explain. Please do not read a full summary/all of your notes and comments but present relevant points only.
2. **1-2 minutes - Primary Reviewer** presents ALL **major** problems/questions. Please do not mention specific minor revisions (including mention of minor consent revisions.) Reviewers can note that minor changes will be forwarded to the analyst. Reviewer should simply state that minor revisions will be forwarded directly to the analyst.

(Items 1 and 2 should not take more than 4-5 minutes total.)

3. **1-2 minutes** – Statistics comments.
4. **1-2 minutes - Secondary Reviewer** adds ONLY information **not already covered by primary.** No need to repeat what was already discussed. If no additional issues, state so.
5. **3-5 minutes** - Discussion of controverted issues, one by one.
6. **2 minutes - IRB Chair** states out loud regulatory findings (111 Approval criteria, vulnerable pops criteria, IND/IDE status, HIPAA waiver)

Presenting Amendments (modifications to already approved studies)

1. Provide a brief summary of the study and what the proposed changes are (one to two sentences)
2. Present any major problems/questions
3. Indicate whether the amendment affects the risk-level benefit of the study

Presenting Progress Reports (annual reviews of already approved studies)

1. Provide a brief summary of the study
2. Present any major problems/questions
3. Indicate whether the progress report affects the risk-level benefit of the study

Primary vs Secondary Reviewer

Primary reviewer: Selected on basis of scientific expertise, the primary reviewer conducts an in-depth review of the protocol.

Secondary reviewer: The secondary reviewer, in contrast, focuses on the readability of the consent form.

Questions to consider include:

- Does it make sense?

- Does it accurately portray the actual study design and procedures in a language that can be understood by the subject (8th grade reading level)?

Tips for Reviewing:

1. Establish a review routine by using a systematic approach to review each new protocol in the same way.
2. Read the consent document to understand the important aspects of the study. The consent document should serve as a good introduction to the study protocol. It should also orient you to the overall design of the study.
3. Read the abstract in the IRB application, which provides key aspects of the study.
4. Read the full protocol and supporting materials carefully. The investigator provides the IRB with detailed information such as the study background and rationale, methodology, inclusion/exclusion criteria for subject enrollment, and other documents. Funding documents provide additional information. Take notes as needed.
5. Reread the consent document. Record suggested corrections or questions for the investigator, and ensure that the consent form adequately describes the actual study design and procedures in a language that can be understood by the subject.
6. Contact the staff reviewer if there is information missing that is needed for full board review.

Points to Consider When Reviewing a Project

Being mindful of certain requirements will help you identify ethical and regulatory issues while reviewing the IRB application. Here are some points to consider:

- What are the subjects required to do? Will they take a drug, fill out a survey, or be interviewed about criminal activity? Are the research activities potentially harmful or embarrassing?
- Would you participate in this study, or would you want your parents, children, spouse or other family members to participate?
- Does the study make sense as written? Is it overwhelming with too much jargon or too many details?
- Is the informed consent document easy to understand and an accurate reflection of the study procedures?
- Who are the subjects and are they vulnerable to coercion (e.g. children, prisoners)?
- Is it necessary to keep the identifying information? Is more information being requested than is needed?
- If identifying information is collected, is there a mechanism in place to protect the subjects' identities or other private information? If so, is it adequate?
- Is the information provided in the protocol, consent, and recruitment materials consistent?
- Are there adequate safeguards to protect the subjects if an untoward event occurs? What action will the PI/researchers take if something goes wrong?
- If the intervention/treatment proves beneficial, will those subjects not in the intervention/treatment group (i.e. control group) be able to partake in the intervention or receive the treatment once the study has been concluded?

- What “gut” feelings do you get after reading the protocol? Sometimes, something about the study seems questionable and may make you feel uneasy. Express this unease and attempt to get the issue resolved, or vote “no” when the vote is taken.

Chapter 5: Criteria for Approval

When reviewing proposed research, the IRB must consider the 7 regulatory requirements, provided below. Among the concepts that must be well understood to review human subjects research are informed consent (elements and process), privacy and confidentiality, and risk and benefit. The information below is not all inclusive and is provided to establish familiarity with these critical topics.

The IRB, or authorized reviewer (in the case of expedited reviews), must determine that the following requirements are satisfied before non-exempt research can be approved. These criteria, as defined in [45 CFR 46.111](#) and [21 CFR 56.111](#), will be considered during the review process for each non-exempt protocol submitted for review.

1. Risks to subjects are minimized: (i) by using procedures which are consistent with sound research design and that do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result from the study. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (i.e., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
3. Selection of subjects is equitable: In making this assessment, the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, individuals with impaired decision-making ability, or economically or educationally disadvantaged persons.
4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative (LAR), in accordance with, and to the extent required by, [45 CFR 46.116](#) and [21 CFR 50.25](#).
5. Informed consent will be appropriately documented, in accordance with, and to the extent required by, [45 CFR 46.117](#) and [21 CFR 50.27](#).
6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

In addition, IRB review will consider the following, as applicable:

1. Recruitment methods and advertising material are appropriate.
2. Payment to subjects
3. Additional protections are in place for vulnerable subjects.

1. Risks to Subjects are Minimized

This criterion is met by first identifying all potential risks (including physical, social, emotional, and those related to breach of confidentiality) in the research study based on prior data or other relevant information. The review of risks begins with contemplation of the potential harms described by the investigator in the iRIS

submission. The IRB reviewer must also consider, based on his/her knowledge and experience, risks that may not be described in the protocol submission. In particular, for all studies that involve greater than minimal risk, the IRB will consider whether the protocol includes provisions by which risks to subjects are minimized and any methods that may decrease risk.

Risks to subjects may be minimized by:

1. using procedures that are consistent with sound research design;
2. using procedures that do not unnecessarily expose subjects to risk, such as reducing or eliminating an exposure;
3. whenever appropriate, using procedures already being performed on the subjects for diagnostic or treatment purposes;
4. increasing monitoring of the subjects for earlier detection of risks or harms; and adding endpoints to the study to reduce further exposure;
5. allocating adequate time to conduct and complete the research;
6. ensuring that adequate facilities are available;
7. when indicated, consideration of whether an adequate number of qualified staff are included;
8. having access to a population that will allow recruitment of the necessary number of subjects;
9. ensuring the availability of medical or psychosocial resources that subjects may need as a consequence of the research.

The IRB process may also minimize risk through requirements for reporting, e.g., authorizing an approval period of less than one year or after a specific number of subjects have been enrolled, or requiring period reports of the progress of the research.

At the time of initial review, an IRB will classify the risk level of each protocol reviewed at a convened meeting, based on information provided in the submission and knowledge/experience of Board members, as minimal risk or greater than minimal risk.

Consideration is given to all measures taken to minimize risk when making the risk level determination.

By definition, protocols that are approved via expedited review under one or more of the federally designated expedited review categories may present no more than minimal risk to subjects.

At each subsequent continuing review, the Board will also consider the status of the study and reported unanticipated problems, and will carry the initial determination forward unless noted otherwise in the IRB record. Changes proposed in modification submissions must also be evaluated for effect on the risk level of the overall study.

Level of review required may change upon subsequent reviews if the risk level changes, e.g.:

1. if the initial submission qualified for expedited review, and a modification increases the risk level to greater than minimal, the protocol would then require full Board review;
2. if the initial submission required full Board review, and procedures were limited to data analysis of long-term follow-up at the time of continuing review, the protocol could then be reviewed under an expedited review procedure.

2. Risk/Benefit Ratio is Acceptable

The IRB will approve a protocol only after it is assured that the risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and to the importance of the knowledge that may be expected to result from the study.

Toward that end, the IRB must:

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

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

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

In evaluating risks and benefits, the Board should consider only those risks and benefits that may result from the research as distinguished from risks and benefits of therapies that subjects would receive even if not participating in the research. The Board should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

Risk

Risk is defined as the probability of harm or injury (physical, psychological, social, or economic) occurring as the result of participation in a research study. Risks also include possible breaches of confidentiality. Both the probability and magnitude of possible harm may vary from minimal to significant.

Physical Harms

Medical research often involves exposure to pain, discomfort, or injury from invasive medical procedures, or harm from possible side effects of drugs. All of these should be considered "risks" for purposes of IRB review. Some of the adverse effects that result from medical procedures or drugs can be permanent, but most are transient. Procedures commonly used in medical research usually result in no more than minor discomfort (e.g., temporary dizziness, the pain associated with venipuncture). Some medical research is designed only to measure more carefully the effects of therapeutic or diagnostic procedures applied in the course of caring for an illness. Such research may not entail any significant risks beyond those presented by medically indicated interventions. On the other hand, research designed to evaluate new drugs or procedures may present more than minimal risk, and can cause serious or disabling injuries.

Psychological Harms

Participation in research may result in undesired changes in thought processes and emotion (e.g., episodes of depression, confusion, or hallucination resulting from drugs, feelings of stress, guilt, and loss of self-esteem). These changes may be transitory, recurrent, or permanent. Most psychological risks are minimal or transitory, but IRBs should be aware that some research has the potential for causing serious psychological harm.

- Subjects may feel stress caused by certain research questions or procedures such as surveys or face-to-face interviews. Some questions may raise painful memories or unresolved issues. Questions about at-risk behaviors may cause embarrassment, feelings of guilt, or legal liability when that behavior is generally illegal or socially unacceptable.
- Provisions for psychological support and referrals can be built into studies when emotional distress may be an outcome. Consent forms describing the kinds of questions the researcher will ask allows participants to choose whether they are comfortable with answering certain types of questions or exploring certain issues.
- A breach of confidentiality may be damaging to a subject's reputation, their employability may be negatively affected, and/or their ability to obtain insurance coverage may be jeopardized if confidentiality is not maintained.
- Information about certain behaviors may place subjects at risk of legal action. For example, if a researcher asks parents how they discipline their children, information about child abuse may be obtained and must be reported. Similarly, if subjects divulge information about illegal activities or stigmatized activities, any disclosure of that information could place the subjects at risk of significant harm.

Benefit

Defined as a valued or desired outcome; an advantage. The benefits of research fall into two major categories: benefits to subjects and benefits to society. Frequently, the research subjects are undergoing treatment, diagnosis, or examination for an illness or abnormal condition. This kind of research often involves evaluation of a procedure that may benefit the subjects by ameliorating their conditions or providing a better understanding of their disorders. Patients and healthy individuals may also agree to participate in research that is either not related to any illnesses they might have or that is related to their conditions but not designed to provide any diagnostic or therapeutic benefit. Such research is designed principally to increase our understanding and store of knowledge about human physiology and behavior. Research that has no immediate therapeutic intent may, nonetheless, benefit society as a whole. These benefits take the form of increased knowledge, improved safety, technological advances, and better health. The IRB should assure that the anticipated benefits to research subjects and the knowledge researchers expect to gain are clearly identified.

3. Scientific Merit

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

1. The research uses procedures consistent with sound research design;

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

When a protocol has undergone a peer review or equivalent process (e.g., for NIH or NSF funding), the IRB will generally accept that the design is sound. When there is an IDE or IND for the study, the IRB may consider the scientific scrutiny of the FDA as confirmation of scientific merit.

For investigator-initiated unfunded projects, unless they have been reviewed by the FDA for the purposes of an IND or IDE application, the IRB must consider the design, to the degree necessary to ensure that statistically valid results may be possible. In making this determination, the IRB may draw on its own knowledge and disciplinary expertise. In general, investigator-initiated protocols that have not received a full peer review receive an additional review by a statistician.

If the research involves investigational products, the IRB must ensure the evaluation of the available nonclinical and clinical information on an investigational product is adequate to support the proposed clinical trial.

In all cases, where the design is such that no generalizable results may emerge, and subjects are placed at risk due to participation, the IRB may not approve the protocol until the design is revised to bring about an acceptable risk/benefit ratio.

4. Selection of Subjects is Equitable

The Board will determine that selection of subjects in each study is equitable, taking into account the purposes of the research, the setting in which the research will be conducted, recruitment methods, and inclusion/exclusion criteria.

At the time of initial review, the characteristics of the anticipated subject population (e.g., ethnicity, race, gender, or vulnerable population) must be considered to ensure that one group does not assume the risks of the research while another group accrues the benefits. Special consideration must be provided for the recruitment of vulnerable populations who may be subject to undue influence or coercion, such as children, prisoners, and individuals with impaired decision-making ability, so that their enrollment and participation in the study is not adversely affected, or risk of procedures increased, by their vulnerability.

5. Informed Consent Process is Appropriate

Informed consent is the process of informing potential subjects about the key facts of a research study and what their participation will involve. The human subjects in the study must participate willingly, after having been adequately informed about the research.

Consent documents must be clearly written and at a level understandable by the subjects. The language must be non-technical (comparable to the language in a newspaper or general circulation magazine). Scientific, technical, and medical terms must be plainly defined. It is often recommended that the informed consent be written at the sixth to eighth grade reading level. Assent forms for minors and any related recruitment materials must reflect the reading level of the minors. The informed consent must be translated into the primary language of the subject if he/she is not fluent in English.

There are three types of consent:

- Consent – An adult subject, capable to give permission to participate in a research study, can provide consent. The subject must be 18 years of age and competent to make the decision to participate.

- Parental Permission – When children/minors are included in research, the parent/guardian must sign a parental permission consent document. Some situations require permission from at least one parent, while other situations require permission from both parents. In some cases, waiving the requirement to obtain parental permission may be necessary. Refer to 45CFR46 subpart D for more information.
- Assent – Assent is a child’s affirmative agreement to participate in research. If the subject is 7-17 years of age, assent must be obtained. The assent form must include simple language written at the appropriate reading level of the youngest subject in the age range.

Further details of the required elements of consent, related information about the process of

informed consent, and the requirements for a waiver of consent can be found in the document “Informed Consent Guidelines.”

6. Documentation of Informed Consent is Appropriate

Use of a written consent form that requires a signature from the subject is the usual means of documenting agreement to participate in studies that involve human subjects. The form generally includes information about the consent process (i.e., describes that the prospective subject should have the opportunity to ask questions and have them answered prior to agreeing to participate), in addition to required elements of consent, and the signed document, becomes a record of the subject’s consent for both the research team and the subject. Procedures usually include plans for subjects to receive a copy of the consent form as well. In clinical studies that involve in-patients, documentation of the subject’s agreement to participate in a research study should also be documented in the medical record. The IRB will determine that the protocol includes procedures to ensure that informed consent will be appropriately documented in accordance with and to the extent required by [45 CFR 46.117](#) and [21 CFR 50.27](#).

In certain specific situations, the requirement for written documentation of informed consent, parental permission, or assent may be waived, as described in the “Informed Consent Guidelines Document.”

7. Data and Safety will be Monitored

Per federal regulations [45 CFR 46.111\(a\)\(6\)](#) and [21 CFR 56.111\(a\)\(6\)](#), the IRB must determine that, when appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

The Einstein IRB will review the data safety monitoring plan for protocols involving more than minimal risk during initial review and at continuing review. For further information on the required elements of data safety monitoring plans, please see the Data and Safety Monitoring Policy document.

At the time of continuing review, interim reports from data and safety monitoring bodies and a summary of UPs to date will be reviewed by the IRB if applicable to the study. Reports that indicate increased risk to subjects or that require changes to the protocol are required to be submitted immediately as a reportable event. The IRB may suspend or terminate research for which the risk/benefit ratio has shifted from acceptable to unacceptable due to the type, frequency, or severity of adverse events or other problems encountered during the conduct of the research.

8. Privacy and Confidentiality will be Protected

The protection of privacy and confidentiality are important issues in the protection of human research subjects. The investigator must describe plans to protect the subject’s identity as well as the confidentiality of

the research records. Privacy and confidentiality are extensions of the principles of autonomy (respect for persons) and beneficence from the Belmont Report.

At the time of initial review, the IRB should ensure that each protocol includes provisions for protecting the privacy of subjects and maintaining the confidentiality of study data. The IRB should consider privacy and confidentiality protections that will be in place during recruitment (e.g., by review of the recruitment plan), enrollment (e.g., by considering whether the subject being seen by others in association with the researcher could result in harm to the subject), and participation (e.g., by examining the extent of electronic security measures to be used to protect data). Details of where paper records will be stored, how electronic data will be protected from unauthorized access, and where data may be transmitted are required in the submission. In addition, consideration should be given to whom has access to the data.

Privacy

Care should be taken to explain the mechanisms that have been devised to protect the privacy of the subjects. The concept of privacy relates to the means for obtaining the data from subjects. For example, when a researcher is interviewing a participant, they must make provisions to protect what is being discussed. Holding the interview in a private office is one method to protect the participant's privacy. Another consideration for privacy is limiting the data being obtained to essential data only. For example, collecting information not related to the research hypothesis is inappropriate.

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

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

Confidentiality

Pertains to the treatment of information that an individual has disclosed in a relationship of trust with the expectation that it will not be divulged to others (without permission) in ways that are inconsistent with the understanding of the original disclosure.

The investigator must provide a plan to keep research records confidential. For example, storing research records in locked file cabinets and password protecting electronic files helps to ensure confidentiality. Investigators should also describe, in their IRB application, who has access to the research records. Without appropriate safeguards, problems may arise from a long-term retention of records. In some cases, to prevent potential criminal or civil prosecution of the research subjects, the IRB may require the destruction of all data that can identify the subjects. Subjects should be informed of whether the data collected will be retained, and if so, for what purpose and for what period of time. Video and audio taped data, as well as photographs require specific plans for confidentiality since these media can provide additional means for subject identification.

In reviewing confidentiality protections, the IRB should consider the nature, probability, and magnitude of harms that would be likely to result from a disclosure of collected information outside

the research. It should evaluate the effectiveness of proposed de-identification techniques, coding systems, encryption methods, storage facilities, access limitations, and other relevant factors in determining the adequacy of confidentiality protections.

9. Recruitment Methods and Advertisements are Appropriate

The IRB will review proposed methods of recruitment, to ensure that the process is not affected by elements of coercion or undue influence, and that the principle of justice, as it relates to availability of innovative practices and sharing of both the burdens and risks of research, is upheld. In addition, the IRB will be mindful that patients coming for clinical care, and the physicians who are responsible for their care, expect that the integrity of the clinical relationship will be respected and taken into account in the research process.

The investigator will provide the IRB with all recruiting materials to be used in identifying participants. The IRB must approve any and all advertisements prior to posting and/or distribution.

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

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

Any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest.

10. Payment to Subjects is Appropriate

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

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

Credit for payment should accrue and not be contingent upon the participant completing the entire study. Any amount paid as bonus for completion of the entire study should not be so great that it becomes unduly influential.

11. Additional Protections are in Place for Vulnerable Subjects

Prior to initial approval of a protocol, and at each continuing review, the IRB will determine that there are appropriate additional safeguards included in the protocol to protect the rights and welfare of subjects who are likely to be vulnerable to coercion or undue influence, e.g., children, prisoners, or individuals with impaired decision-making capacity.

Federal regulations outline special protections for specific populations such as prisoners or children. In addition, IRBs and researchers must bear in mind that vulnerability extends beyond regulatory definitions. Vulnerability is an important consideration in all IRB deliberations. Individuals, as well as entire cohorts of subjects, may be susceptible to coercion depending on the particular study. Adequate justifications must be provided for studies that enroll vulnerable subjects.

Chapter 6: Post-Approval Submissions

After a research project is approved, there are many situations requiring communication with the IRB during the conduct of the research. These communications result from events that unfold (and may or may not be expected) as the research is taking place. Investigators are required to submit reports or communication on: adverse events, unanticipated problems, changes, study continuing reviews, expiration of approval period, study completion, and terminations/suspensions. This chapter provides an introduction to each of these sections.

Reportable Events: Adverse Events and Unanticipated Problems

After a potential Unanticipated Problem occurs, the principal investigator is required to submit a reportable event form to the IRB through the iRIS system. These reports must be submitted within 5 days of becoming aware of the problem.

The principal investigator's report should contain enough information for the IRB to determine whether the event increases the level of risk to participants, requires a research design change, or necessitates modification to the informed consent form.

Definitions

Adverse Event: Any untoward or unfavorable medical occurrence in a human subject, including abnormal signs (for example, abnormal physical exam or laboratory finding), symptoms, or disease, temporally associated with, but not necessarily considered related to, the subject's participation in the research study. Not all adverse events meet IRB reporting guidelines.

Serious Adverse Events (SAEs) are those that: are fatal or life threatening, result in significant or persistent disability, require or prolong hospitalization, result in a congenital anomaly/birth defect, or in the opinion of the investigators, represent other significant hazards or potentially serious harm to research subjects or others.

Unanticipated Problem (UP): any incident, experience, or outcome that meets all of the following criteria:

- A. unexpected (in terms of nature, severity or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- B. related or possibly related to participation in the research (possibly related meaning there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and,
- C. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic or social harm) than was previously known or recognized.

The Einstein IRB also requires investigators to report various other events, such as unresolved subject complaints or protocol deviations that may place subjects at increased risk. For a full list of reporting requirements, refer to the policies "Research Noncompliance," "Unanticipated Problems," and "Other Reportable Events."

Changes to Previously Approved Research

Any proposed change to a previously IRB approved research project must be submitted to and approved by the IRB before the change is implemented, except when necessary to eliminate apparent immediate hazards to the subjects. Amendment submissions can be reviewed by the expedited review procedure or require review by the fully convened IRB depending on the assessment of associated risk. Typically, minor changes are reviewed by the expedited procedure. Minor changes do not alter the risk/benefit ratio in previously approved research (e.g. correction of typos, adding investigators to the project, etc.).

All investigators proposing modifications to a previously approved human subject research project must submit an amendment form via iRIS. The amendment form serves as a “cover letter” that lists/details the proposed changes to the study. In addition to the amendment form, investigators must make the changes to the originally submitted documents. In reviewing amendments, the IRB analyzes whether the changes pose additional risks to subjects or represents a significant change in study procedures. The IRB may impose additional contingencies before approving the amendment.

Continuing Review

Research protocols undergo continuing review at intervals appropriate to the degree of risk, but not less than once per year.⁷ The frequency and extent of continuing review for each study is based upon the nature of the study, the degree of risk involved, the novelty of the research procedures, and the vulnerability of the study’s subject population. After a careful consideration of each of these factors, each protocol is assigned an approval period, after which the study must be re-reviewed by the IRB. In some instances, such as the use of innovative procedures/techniques (i.e. surgical procedure), the IRB may choose to grant an approval period based on number of subjects accrued, rather than on a specific time period. ***This type of approval is usually assigned when there are significant concerns regarding the potential risks of participation.***

Each investigator must abide by the approval period imposed by the IRB at the time of the most recent IRB approval. Each IRB approval notice designates a period of time during which activities involving human research subjects may be *undertaken*. No research project may continue to recruit, enroll, or treat subjects or analyze data after the IRB approval expiration date (except where doing so would cause harm to the subjects).

It is the investigator’s responsibility to ensure that approval for an active protocol remains current. The IRB expiration date can be found on the protocol summary view in the iRIS system. The investigator must submit a progress report form through iRIS prior to expiration in order to renew the approval period.

Expiration of Approval Period

If the investigator does not submit a progress report form through iRIS by the current expiration date, the investigator is notified by e-mail that IRB approval has expired. The email includes a notice that all study related activities must cease (including recruitment, enrollment, interventions, interactions, or data analysis). After 6 months, IRB staff administratively close the study.

In the event that a protocol expires and the withdrawal of research interventions may place study subjects at risk, the investigator may request that the IRB grant permission to allow the continuation of activities required for subject safety prior to renewal of IRB approval. If subject safety would be compromised by study closure, investigators can request that the IRB allow continuation of study activities for currently enrolled

⁷ There is an exception for “exempt” research, to which human subjects regulations do not apply. We assign three year approval periods for such exempt research. However, such exempt research is reviewed administratively by OHRA staff, and does not get reviewed at the IRB meetings.

subjects. If research-related interventions have been continued with subjects on an expired protocol, the IRB must be immediately informed of the circumstances that necessitated this action by means of a Protocol Exception request.

Requests justifying continuation of currently enrolled subjects will be forwarded to an IRB Chair for consideration. If the IRB Chair grants permission to allow the continuation of research interventions with previously enrolled subjects for reasons related to subject safety, the IRB will send written notification to the investigator. Other research activities (such as recruitment, enrollment, data analysis, etc.) may only be resumed after the investigator receives continuing approval for the research.

Study Completion

A research project is closed when subject accrual, subject follow-up, and data analysis are completed. Once a study is closed, no further research activity, including data analysis, may occur.

Upon study completion, the investigator should submit a progress report through iRIS, indicating the study status as “closed”. By doing so, the researcher confirms that the study is finished and that no further interactions with subjects or their data will take place. Once the study is closed in iRIS, the researcher is no longer required to submit yearly continuing review applications. If the investigator wishes to enroll new subjects for the closed study, he/she must reactivate the protocol with the IRB. The IRB, in consultation with the principal investigator, may consider closing a study when active data analysis and publication pursuant to the approved study has ceased, even if the investigator retains records that may identify individual subjects. Additional research projects using data acquired in the approved study may constitute new human subjects research studies subject to separate IRB review.

Termination/Suspension of a Study

Termination is when the IRB permanently withdraws approval of ALL research activities for a particular study. Terminated research is no longer required to undergo continuing review. Suspension is when the IRB temporarily or permanently withdraws approval of some or all research activities. Suspended research is still under the jurisdiction of the IRB and still requires continuing review.

If there is an urgent situation requiring suspension of all or part of a study, the Executive Chair or OHRA Director may make this determination. If the Executive Chair or OHRA Director suspends a study on his/her own, the IRB is notified by the Chair at the next IRB meeting. The decision to terminate a study’s approval must be made by the convened IRB.

Chapter 7: iRIS Instructions

Accessing iRIS:

Log in at <https://iris.einsteinmed.org> using your MMC credentials.

Activating account:

Email your username, department/division name to the iRIS Support requesting account activation.

iRIS Support Team: iris-support@einsteinmed.org

Email address:

Confirm that your correct email address is listed in iRIS. To check your email address go to My Assistant → My Account Information → Profile. If your email address is not listed, outdated or incorrect, contact Montefiore and **ask them to open a ticket with IT Security** to correct your email address in the '*mmcYUemail*' attribute field.

Montefiore IT: (914) 881-4554 or itservicedesk@montefiore.org

Checking CITI training status:

Confirm that your CITI training is active and showing in your iRIS profile. Click on My Assistant → My Account Information → Training History. If there is nothing listed under this section, contact the iRIS Support Team

Viewing the IRB meeting agenda:

- Click on Einstein IRB Assistant → Select Committee (East or West) → Meeting Agenda.
- Click on the notepad under the column titled “Click to open” to view the submissions.
- Click on “Submission Components” to view the documents associated with the submission.

Notification of Review Assignment:

When you are assigned a review, you will receive an automated email from the iRIS system with the subject line stating: “IRB Notification: Review Assignment”

You will also receive a separate email with the review information in body of the email. This is sent from the IRB analyst who is assigned to the submission.

- The IRB analyst who is assigned to your submission should be included in ALL EMAIL COMMUNICATION regarding your review.

Completing reviewer’s checklist:

- Login to iRIS
- Under the heading “Below are your incomplete Einstein IRB tasks” there is a “Review Assignments” folder with a blue arrow

- The blue arrow must be pointing in the up direction in order to see the assignment (s)

Below are your incomplete Study tasks:

Below are your incomplete Einstein IRB tasks:

 Reviewer Assignment [Open Dashboard](#) 1

1 task(s) found... 1 - 1

Open	Principal Investigator	IRB Number	Study Alias	Study Status	Submission Form Name	Submission Date	Review Process	IRB Initial Approval	Expiration	Received
	Life Course Research to Identifying Longevity Phenotypes and Genotypes									
	Sofiya Milman	2018-9258	LifeLong	Open	Submission Response for Amendment Form	08/19/2019	Expedited	09/05/2018	08/04/2020	08/30/2019

- Select the notepad icon under the column “Open”
- Select “IRB Board Member/Consultant/Statistician and press “Save and Continue to Next Section” to proceed through each section of the checklist.
- When review is complete, select “YES” to the question “Is your review complete?”
- Click on “Click here to sign the document”
- iRIS will prompt you to enter your username and password
- When complete click “Save Signoff”

Appendix A: Glossary of Common Terminology

Abstention An abstention is neither a "yes" nor a "no" vote and is cast when a member is not comfortable in voting either way. Any member is free to abstain at any time. An abstention counts toward quorum but does not count toward a super majority.

Adverse Event/Effect (AE) Any untoward physical or psychological occurrence in a subject participating in research. An AE can be any unfavorable or unintended event including an abnormal laboratory finding, or a symptom or disease associated with the research. Adverse events may or may not have a causal relationship with the research.

Approved Drug / Device An approved drug/device means the drug/device being studied has been cleared by the U.S. Food and Drug Administration (FDA) for marketing.

Assent Agreement to participate in research obtained from an individual not competent to give legally valid informed consent (e.g., a child or cognitively impaired person). An assent form is like an informed consent form but is tailored to the status/age of the individual not competent to give consent. It is only binding in conjunction with parent/guardian consent.

Audit A systematic and independent examination of research activities and documents, to verify that the activities were conducted according to the protocol, sponsor's expectations, institutional procedures, good clinical practice (GCP), and applicable regulatory requirement(s).

Autonomy Personal capacity to consider alternatives, make choices, comprehend information, and act without undue influence or interference of others.

Belmont Report The National Commission for the Protection of Human Subjects in 1978 authored the Belmont report. It establishes the basic ethical principles for conducting human subjects research: autonomy, beneficence, and justice.

Beneficence Beneficence is an ethical principle discussed in the Belmont Report that entails an obligation to protect persons from harm. The principle of beneficence can be expressed in two general rules: (1) do not harm; and (2) protect from harm by maximizing possible benefits and minimizing possible risks of harm.

Benefit A benefit is a valued or desired outcome; an advantage.

Bias When objectivity is impaired by personal gain or personal judgment. In clinical studies, bias is minimized by blinding and randomization.

Biologics Biologics, as regulated by the U.S. Food and Drug Administration, include therapeutic serum, toxin, anti-toxin or microbials used for the prevention, treatment, or cure of diseases or injuries.

Blinded Study Design Study designs comparing two or more interventions in which the investigators, subjects, or some combination thereof do not know group assignments.

Case Report Form (CRF) A printed, optical, or electronic document designed to record regulatory and protocol-required data from each individual enrolled in the study. The CRF is reported to the sponsor for each subject and also provides documentation for quality assurance and monitoring.

Clinical Trial A clinical trial is a research study to evaluate the safety and efficacy of vaccines, new therapies, or new ways of using known treatments. Clinical trials are often staged (e.g., phase I, II, III) to learn essential information putting fewest subjects at risk.

Coded Information Coded means replacing identifiable information (such as name or social security number) with a number, letter, symbol, or combination thereof (i.e., the code).

Cognitively Impaired Having a disorder (psychiatric or developmental) that affects cognitive or emotional functions that impair the capacity for sound judgment and reasoning. Other conditions that may impair judgment and reasoning are: being under the influence of drugs or alcohol, having a degenerative disease, having a terminal illness or having disabling handicaps.

Cohort In epidemiology, a group of individuals selected for common characteristics.

Community Based Clinical Trial (CBCT) A clinical trial conducted primarily through primary-care physicians rather than academic research facilities.

Community Member/ Non-Affiliated Member A member of an Institutional Review Board who has no ties to an institution, its staff, or faculty. This individual is usually from the local community (e.g., minister, business person, attorney, teacher, homemaker, etc.).

Compassionate Use A method of providing experimental therapeutics prior to the final FDA approval. This allows treatment for sick individuals who have no other options. Often, case-by-case approval must be obtained from the FDA for "compassionate use" of a drug, therapy or device.

Compensation Payment for participation in research.

Competence (Capacity to consent) A legal term used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice.

Compliance Adherence, in this case, to federal regulations, state laws, institutional policies and sponsor requirements.

Confidentiality Pertains to the handling of information/data that an individual has disclosed in a relationship of trust. The expectation is that the information/data will not be divulged to others without permission, or in ways that are inconsistent with the original disclosure.

Conflict of Interest (COI) Management Plan Management plans are issued by Einstein's COI committee and describe the limits of a researcher's ability to serve as PI or a member of a study team. Management plans define a relationship between a researcher and a company. The management plan also describes the disclosures required in consent forms and publications that result from the study. One researcher may have multiple management plans.

Continuing Review Periodic review of a research study by an IRB to evaluate whether risks to participants remain reasonable in relation to potential benefits and to verify the study continues to meet regulatory and institutional requirements. Continuing review shall be conducted at intervals appropriate to the degree of risk but not less than once per year. ([45 CFR 46.109\(e\)](#); [21 CFR 56.109\(f\)](#))

Contract An agreement that a specific research activity will be performed under the direction of an entity providing funds. Research performed under a contract is more closely controlled by the entity than research performed under a grant.

Contraindication A specific circumstance when the use of certain treatments is not recommended.

Control/Normal Subject(s) Subject(s) who do not receive the treatment being studied, who are then used for comparison to subjects who do receive the treatment. Or, subjects who do not have a given condition, background, or risk factor that is being studied.

Controlled Study Research that involves at least two groups: one that receives the study intervention and the other that receives a placebo or another intervention. These studies are also referred to as “blind” / “masked” (i.e. the subjects do not know which treatment they are receiving) or “double blind” / “double-masked” (i.e. neither the subjects nor the researchers know the treatment assignments).

Cross-Over Design A type of clinical trial in which each subject experiences, at different times, both the experimental and control therapy. For example, half of the subjects might be randomly assigned first to the control group and then to the experimental intervention, while the other half would have the sequence reversed.

Data Analysis The process of applying statistical techniques to describe, summarize, and compare data to extract useful information and facilitate conclusions.

Data and Safety Monitoring Board (DSMB) An independent committee that collects and analyzes data during the course of a clinical trial to monitor for adverse effects and other trends that would warrant changes or early closure of the trial.

Debriefing Providing subjects with previously undisclosed information about the research project or the study’s real purpose.

Deception Deception, when referring to studies, is the intentional misleading of subjects or the withholding of full information about the nature of the study. Deception increases ethical concerns because it interferes with the ability of the subject to give fully informed consent. However, deception is arguably necessary for certain types of behavioral research to prevent biased behavior or answers.

Deferral Submissions to the IRB that: (1) require substantial revisions (e.g., specific wording cannot be provided by the convened IRB); or (2) prompt questions that cannot be answered within the context of the IRB meeting, will be deferred for further review by the convened IRB at a later date.

Design A research design is a plan or analytical approach for answering research questions. Some examples of research designs are experimental, correlational, observational, and single case. The selection of a particular study design depends on the information sought.

Device/Medical Device A diagnostic or therapeutic article that does not achieve any of its principal intended purpose through chemical action within or on the body (which would be considered medicine). Such devices include diagnostic test kits, crutches, electrodes, pacemakers, arterial grafts, intraocular lenses, and orthopedic pins or other orthopedic equipment.

Diagnostic Trials Trials that are conducted to find better diagnostic tests/procedures for identifying a particular disease or condition. Diagnostic trials enroll people who have signs or symptoms of a disease or condition being studied.

Double Blind Study A clinical trial design in which neither the participating individuals nor the study staff knows which trial regimen participants are receiving. Double blind trials are used to increase objectivity so expectations do not influence outcome.

Drug/Pharmaceutical Any chemical compound that may be administered to humans for the diagnosis, treatment, cure, mitigation, or prevention of disease or of benefit to other conditions.

Efficacy The ability of a drug or treatment to produce the expected result.

Eligibility criteria These are defined requirements for subject inclusion/exclusion in a given experiment. Eligibility criteria examples are age, sex, state of health, a defined range for a biologic measure (e.g. glucose level or cholesterol), blood cell counts, etc.

Empirical Based on experimental data; not theory.

Endpoint A target outcome of a trial. Endpoints are chosen because they are measurable.

Engagement of Institutions in Research An institution becomes "engaged" in human subjects research when its employees or agents (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes.

Equitable The fair or just selection of study subjects (principle of justice) to assure that the benefits and burdens of research are equally distributed.

Ethnographic/Fieldwork/Anthropology Research Ethnography is the study of people and culture. Ethnographic research involves observation of a person or group studied in their own environment, often for long periods of time.

Exempt Research Exempt research is Human Subjects Research that meets one of the minimal risk categories in the federal regulations.

Expanded Access Increasing the inclusion criteria in an experimental drug study to allow for enrollment of participants who are failing on currently available treatments, and/or are unable to participate in any other ongoing clinical trials.

Expedited Review A review undertaken per federal regulations by the IRB chair or a designated voting member, rather than the entire IRB.

Experimental Drug A drug that has an Investigational New Drug (IND) application filed with the FDA, but has yet to be licensed.

Federal Wide Assurance (FWA) An agreement between a federally funded entity and the HHS Office of Human Research Protections (OHRP) that stipulates methods by which the entity will protect research participants (66 Fed Reg 19139, 19141 April 13, 2001.). Non-HHS federal agencies also use the assurance process for their funded entities.

Fetus A developing human from two months after conception to birth. If the delivered or expelled fetus is viable, it is designated an infant [45 CFR 46.203(c)]. The term "embryo" is usually used for earlier phases of development.

Food and Drug Administration (FDA) Along with the Office of Human Research Protections (OHRP), the Food and Drug Administration (FDA) is the other regulatory body with oversight authority over research with human subjects. FDA oversight extends to all research with human subjects involving investigational drugs, devices and biologics, regardless of funding source. The FDA is a division of the U.S. Department of Health and Human Services (DHHS), and FDA auditors can inspect the Einstein IRB's records involving FDA regulated studies at any time. (<http://www.fda.gov/>).

Full Board Review Review of proposed or continuing research (primarily greater than minimal risk research) by a convened IRB meeting, at which a majority of the voting membership is present.

Gene Therapy The treatment of certain disorders, especially those caused by genetic anomalies or deficiencies, by introducing specific engineered genes into a patient's cells.

Genetic Screening Genetic tests or methods to identify persons who have a gene that is thought to be linked to a certain phenotype or who are at risk of inherited diseases or disorders.

Guardian An individual who is authorized under applicable state or local law to give permission on behalf of a child or make decisions for an incompetent adult [[45 CFR 46.402\(c\)](#)].

Grant Financial support provided for a research study. Fund givers typically do not exercise strict control over the grants they have awarded.

Health Insurance Portability and Accountability Act (HIPAA) HIPAA's Privacy Rule of 2003 prohibits health care providers such as health care practitioners, hospitals, nursing facilities and clinics from disclosing protected health information without written authorization from the individual (HIPAA Authorization).

Human In Vitro Fertilization Fertilization involving human sperm and ova that occurs outside the human body (e.g. a test tube).

Human Research Protection Program (HRPP) The Human Research Protection Program (HRPP) is the total of all departments and individuals responsible for the protection of human research subjects. At Einstein, the HRPP consists not only of the Office of Human Research Affairs and the IRB, but also the OCT, OSRP, IBC, ICTR, and the entire research community. The HRPP is headed by the Institutional Official (IO).

Human Subjects Under the federal regulations (45 CFR 46), human subjects are defined as: living individual(s) about whom an investigator conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information.

Identifiable Personal Information Data containing enough information to reveal the identity of the subject.

Inclusion/Exclusion Criteria The pre-determined conditions of a clinical trial that allow or exclude participation. These criteria are factors such as age, gender, type and stage of a disease, previous treatment history, and/or other medical conditions.

Investigational Device Exemptions (IDE) Investigational devices that are exempt from regulations found in the [FDA Medical Device Amendments](#) because of their low risk profile. This allows such unapproved devices to be used in clinical investigations such as IDE.

Investigational New Drug or Device (IND) A drug or device permitted by FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing.

Informed Consent A person's voluntary agreement – based upon adequate knowledge and understanding of relevant information – to participate in research or undergo a diagnostic, therapeutic, or preventive procedure.

Informed Consent Document A document that provides prospective participants with the purpose, procedures, potential risks and benefits of involvement in a research study, as well as alternatives to participating. This document is also what participants sign to demonstrate their consent to participate in research.

Institutional Official (IO) An officer of an organization who has the authority to speak for and legally commit the entity to comply with federal regulations regarding the involvement of human subjects in research.

Institutional Review Board (IRB) To protect the welfare of human subjects participating in research, a specially constituted review body designated by an entity to review human subject research protocols.

International Studies Procedures and policies that apply to research taking place outside the U.S. often differ from those set forth in the U.S. federal policies. U.S. federally funded research activities in a foreign country may be approved only if the ethical protections are equivalent to those in the U.S. This is also true for FDA approval of drugs/devices/biologics tested outside the United States.

Investigator Initiated Research Research that is initiated and conducted by an individual rather than a sponsor/pharmaceutical company. The investigator has the same responsibilities that a sponsor would have.

Investigator's Brochure A compilation, created by the sponsor of all the clinical and nonclinical data on the investigational product(s).

In Vitro Refers to processes occurring outside of a living organism.

In Vivo Refers to processes carried out within a living organism.

IRB Records IRB records include but are not limited to: minutes from IRB meetings, proposals reviewed, amendments, investigator brochures, and supplemental information including recruitment materials, consent forms, continuing reviews, correspondence, and IRB membership.

iRIS The online system through which all Einstein and Montefiore IRB applications are submitted, reviewed, and approved.

Key Personnel Key Personnel are the individuals who have access to Protected Health Information (PHI) and generate data either through direct interactions with subjects or through access to their medical records. Key Personnel and their study roles must be listed on an IRB submission.

Justice An ethical principle discussed in the Belmont Report requiring fairness in the equitable distribution of burdens and benefits within the study population.

Legally Authorized Representative An individual, judicial, or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

Longitudinal Study A study designed to follow groups of subjects for an extended period of time.

Minimal Risk A risk is minimal when the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests [[45 CFR 46.102\(i\)](#)].

Minor Persons who have not attained the legal age to consent to treatment or procedures in research, as determined under the applicable law of the jurisdiction in which the research will be conducted [[45 CFR 46.401\(a\)](#)].

Monitoring A systematic, ongoing process to evaluate or oversee the conduct of research procedures.

New Drug Application (NDA) The New Drug Application (NDA) is the application drug sponsors submit to the FDA for approval of a new pharmaceutical for sale and marketing.

Non-Significant Risk Device An investigational medical device that does not present significant risk to the research subject (e.g., tongue depressor, or swab).

Non-Viable Fetus An expelled or delivered fetus, which although living, cannot possibly survive to the point of independently sustaining life, even with the support of available medical therapy [[45 CFR 46 203\(d\)\(e\)](#)]. Although it may be presumed that an expelled or delivered fetus is nonviable at a gestational age less than 20 weeks and weight less than 500 grams [*Federal Register* 40 (August 8, 1975):33552], a specific determination as to viability must be made by a physician in each instance.

Off Label-Use A drug used for conditions other than those approved by the FDA.

Office for Human Research Protections (OHRP) The U.S. Department of Health and Human Services office responsible for regulations [[45 CFR Part 46](#)] governing research involving human subjects.

Office of Human Research Affairs (OHRA) at Einstein The Einstein office responsible for the oversight and direction of the Human Subjects Protection Program. This includes administrative oversight of the IRBs, maintenance of institutional Human Subjects Research policies, and setting educational requirements.

Open Label Design An experimental drug trial in which both the investigator(s) and the subjects know the treatment group(s) to which subjects are assigned.

Orphan Drugs An FDA category of medication used to treat rare diseases and conditions.

Peer Review Experts with the same scholarly background as the person submitting a project, who review research for scientific merit, participant safety, and ethical acceptability.

Pharmacokinetics The study of mechanisms of absorption, distribution, metabolism, and excretion of a drug or vaccine.

Placebo A chemically inert substance used in controlled clinical trials to provide data that helps distinguish and determine whether improvement and side effects reflect imagination or anticipation rather than the actual power of a drug.

Placebo Controlled Study A method of investigation of drugs in which an inactive substance (the placebo) is given to one group of participants, while the drug being tested is given to another group. The results obtained in the two groups are then compared to see if the investigational treatment is more effective than the placebo in treating the condition.

Preclinical Refers to the testing of experimental drugs in the test tube or in animals - the testing that occurs before human trials.

Prevention Trials Refers to trials that find improved ways to prevent disease in people who have never had the disease or to prevent a disease from returning. These approaches may include medicines, vaccines, vitamins, minerals, or lifestyle interventions.

Primary Data Collection Primary data collection involves direct contact with, or observation of, one or more people for the purpose of collecting data from or about them.

Principal Investigator (PI) The scientist, scholar, or student with ultimate responsibility for the design and conduct of a research project.

Prisoner An individual confined or detained in a penal entity.

Privacy Control over the extent, timing, and circumstances of sharing oneself (physically or behaviorally) with the PI or other research staff.

Prospective Studies A study designed to follow groups of subjects for an extended period of time with defined outcomes.

Protected Health Information (PHI) PHI is health information transmitted or maintained in any form or medium that includes ALL of the three following parts:

- identifies or could be used to identify an individual; and
- is created or received by a healthcare provider, health plan, or healthcare clearinghouse; and
- relates to the past, present, or future physical or mental health or condition of an individual; the provision of healthcare to an individual; or the past, present, or future payment for the provision of healthcare to an individual.

Protocol The formal design or plan of an experiment or research activity.

Quorum A majority of voting members (50% + 1) who must be present for a convened IRB meeting to proceed. Must be maintained and documented for all votes.

Random, Random Assignment, Randomization, Randomized A method of assigning subjects to different treatment groups based on chance.

Recruitment/Recruitment Materials Recruitment is the process by which potential subjects are informed about a study. Recruitment materials, such as fliers, email messages, newspaper ads, and phone calls, must be accurate, non-coercive, and must not emphasize monetary compensation. These materials must be approved by the IRB.

Reliance Agreement An IRB Reliance Agreement is a written document between Einstein and an external site or individual. It allows the Einstein IRB to extend its IRB oversight to the site/individual for the conduct of a specific study.

Research Systematic investigation, including research development, testing, and evaluation, designed to produce or contribute to generalizable knowledge [45 CFR 102(d)].

Research with Human Subjects Research with human subjects is a systematic investigation using data or samples derived from identifiable living humans that is designed to contribute to generalizable knowledge. Research with human subjects requires IRB review and approval.

Respect for Persons An ethical principle discussed in the Belmont Report requiring that individual autonomy be respected and that persons with diminished autonomy be protected.

Retrospective Studies Research conducted by reviewing records from the past (e.g., birth and death certificates, medical records, school records, or employment records) or by obtaining information about past events elicited through interviews, surveys or measurements.

Risk The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations only define “minimal risk.”

Risk/Benefit Ratio Comparing the potential benefits to the risks of participating in a research study.

Secondary Data Secondary data collection involves accessing information that has already been obtained either individually or in aggregate form.

Serious Adverse Event (SAE) Defined by the FDA as an event that jeopardizes the research subjects and may require medical or surgical treatment (e.g., death, a life threatening experience, hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, congenital anomaly and/or birth defects).

Side Effect Any undesired action or effect of a drug or treatment. Negative or adverse effects may include headache, nausea, hair loss, skin irritation, or other physical problems. Experimental drugs must be evaluated for both immediate and long-term side effects.

Significant Risk Device An investigational medical device that presents a potential for serious risk to the health, safety, or welfare of the subject.

Single-Blind/Blind Study A study in which one party, either the investigator or participant, is unaware of what medication the participant is taking.

Sponsor A person, federal agency, corporation, or other entity that provides funds for a research project.

Standard Treatment / Standard of Care A treatment or regimen in wide use and considered to be effective in the treatment of a specific disease or condition. (Often used as comparator for a new drug, device, biologic or treatment).

Stratification A statistical method used to categorize subjects into subgroups by specific characteristics. This enables researchers to look into separate subgroups.

Study Arm Any of the treatment groups in a randomized trial. Most randomized trials have two “arms” but some have three or more.

Suspension/Termination IRB approval is suspended/terminated and all research activity is halted as the result of: unanticipated problems involving risks to subjects or others, serious or continuing noncompliance with [45 CFR Part 46](#), or the requirements/determinations of the IRB not being followed or met.

Survey A means to obtain information from respondents through written questionnaires, telephone interviews, door-to-door canvassing, or similar procedures.

Toxicity A detrimental effect produced by a drug or condition.

Unanticipated Problem Involving Risks to Subjects or Others (UP) Any event that is unexpected, related or possibly related, and suggests that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized.

Viable Infant When referring to a delivered or expelled fetus, the term “viable infant” means likely to survive to the point of sustaining life independently, given the benefit of available medical therapy [45 CFR 46.203(d)]. In research, this judgment must be made by a physician unaffiliated with the research project.

Voluntary Free of coercion, duress, or undue inducement. Used in the research context to refer to a subject's willingness to participate (or continue to participate) in a research activity.

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

Waiver A waiver or alteration of consent and/or HIPAA authorization is a document approved by the IRB that allows an investigator to forego certain requirements for obtaining consent or HIPAA authorization. It is commonly used to ascertain (identify) potential research subjects by reviewing their private health information prior to their consent.