CHAPTER 2 IREC 101

This chapter provides a short introduction to IREC regulations, policies, procedures, research terminology, and the roles of research personnel. It also provides tips on how to review a protocol.

WHAT POLICIES AND PROCEDURES SHOULD I BE FAMILIAR WITH?

IREC is expected to follow Kazakhstan laws, as well as Nazarbayev University policies. In addition to these requirements, IREC examines ethical issues when reviewing research projects. For NU's IREC, a comprehensive set of policies and procedures is available at https://nu.edu.kz/about-us/institutional-research-ethics-committee. IREC members should familiarize themselves with these policies and procedures and refer to them when completing reviews.

WHAT IS INFORMED CONSENT?

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. If the subjects are from a vulnerable population such as children, additional protections are required.

WHAT ARE THE REGULATORY LEVELS OF IREC REVIEW?

There are three levels of review for human subjects research: exempt, expedited and full board.

Exempt Review: protocols commonly involve less than minimal risk (e.g. anonymous survey) to subjects and fall within at least one of the four defined categories. This level of review has no continuing IREC oversight requirements. The exempt categories are:

- **Exemption 1:** Research conducted in commonly accepted educational settings involving normal educational practices
- **Exemption 2:** Educational tests, surveys, interviews, or observation of public behavior unless subjects can be identified and disclosure of data could place subject at risk
- **Exemption 3:** Collection/study of existing data, documents, records, specimens, if publicly available or if the information is not identifiable
- **Exemption 4:** Research and demonstration projects conducted/approved by Department/Agency heads designed to study/evaluate public benefit or service programs

Expedited Review: protocols involve minimal risk (e.g. blood draw, longitudinal study on attendance and graduation outcomes) and fall within one of six defined categories. These projects are reviewed by one designated, well trained IREC member. This level of review has ongoing IREC oversight requirements. The expedited categories are:

- **Category 1:** Clinical Studies that do not involve an investigational drug or device exemption

- **Category 2:** Blood sample collection (routine methods-small amounts)
- **Category 3:** Prospective collection of biological samples through noninvasive means
- **Category 4:** Data collected through noninvasive means (routinely practiced in clinical settings)
- **Category 5:** Collection of voice, video or digital data for research purposes
- **Category 6:** Individual or group behavior, surveys, interviews

Full Board Review: protocols involving greater than minimal risk (e.g. drug, device, biologics, and collecting/recording private information). These projects are reviewed by a fully convened IREC committee. This level of review is extensive and has continuing IREC oversight requirements.

WHAT ARE THE TYPES OF IREC RESEARCH SUBMISSIONS/INTERACTIONS?

There are a variety of types of IREC submissions and various reasons that may warrant IREC –researcher interaction. The following is a list of the different types of IREC submissions:

Common types of submissions include:

- *Full Board*: more than minimal risk, requires IREC review
- *Expedited*: minimal risk, requires review by one designated IREC reviewer
- *Exempt*: less than minimal risk, can be reviewed by IREC staff
- *Continuing Review*: yearly review required for full board and expedited 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, noncompliance

Other IREC – research interactions include:

- *Suspension*: temporary hiatus of study procedures resulting from decision of IREC, PI, or sponsor
- *Termination*: IREC decision to halt a study, and usually requires a new submission to reactivate

HOW TO REVIEW A PROTOCOL

Using the NU IREC reviewer checklist is the required method to review protocols, support materials, and consent documents. The reviewer checklist helps organize thoughts, provides reminders of issues to be addressed, and gives useful formats to present the review. The complete set of NU IREC reviewer checklists can be found in Appendix A.

Once a member establishes a system for review research that work well for her/him, the process will become easier over time. IREC members may always call the IREC staff or another IREC member if something is unclear, missing or prompts questions about the proper course of action.

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 IREC application which provides key aspects of the study.
4. Read the **full protocol** and **supporting materials** carefully. The investigator provides the IREC 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 IREC secretary or IREC Chair if there is information missing that is needed for full board review.

WHO ARE VULNERABLE SUBJECTS?

The term "vulnerable subjects" refer to research subjects that have been designated as vulnerable by federal regulations. Federal regulations outline special protections investigators must incorporate into their research when enrolling and conducting research with vulnerable subjects. Vulnerable subjects are:

- pregnant women, human fetuses, and neonates
- prisoners
- children

IRECs and researchers must bear in mind that vulnerability extends beyond the regulatory definitions. Vulnerability is an important consideration in all IREC 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.

WHAT CRITERIA MUST BE MET TO APPROVE A PROTOCOL?

The "Common Rule" sets forth certain criteria that must be met in order for the IREC to approve a protocol. Proposed research must satisfy each requirement below:

(1) Minimized Risks

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

(2) Reasonable risk/benefit ratio

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

(3) Equitable subject selection

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

(4) Obtain Informed Consent

Informed consent will be sought from each prospective subject or the subject's legally authorized representative.

(5) Document Informed Consent

Informed consent will be appropriately documented unless documented informed consent is waived

(6) Data monitored for safety

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

(7) Confidentiality/privacy maintained

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

Additional safeguards must be included 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.

WHAT IS CONFLICT 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, IREC 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.

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.

IREC 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. IREC 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, IREC may request a member to be present in order to provide information to the committee. Unless an IREC member declares a conflict of interest, their unbiased ability to review a project is assumed.

THE DIFFERENCE BETWEEN BIOMEDICAL AND SOCIAL/BEHAVIORAL RESEARCH

IREC members may review biomedical or social and behavioral research, or both. IREC will make every effort to review social/behavioral research in an appropriate context. In order to feel comfortable understanding the differences between social/behavioral and biomedical research, the following matrix illustrates some typical differences:

	Social Behavioral	Biomedical
Terms commonly used to describe the research	interpretative, qualitative, action, observational, community based, emergent	quantitative, positivist, objective
Intended Research Outcome	produce rich description or theory	use of controlled/limited variables to test a biomedical outcome
Validity of Outcome Provided by	a research strategy utilizing verification/validation measures and reliable observation techniques	fixed procedures
Interaction with Subjects	social scientist is often an involved participant	researcher is a non-participant
Methods Used	observations, surveys, interviews, focus groups, comparisons, internet	drugs, medical procedures, interventions, test devices, biologics
Hypothesis Driven?	can be yes or no	yes
Interpretation by Experimenter vs. Experiment	experimenter and experiment	experiment
Social Distance between Researcher and Subjects	can be close relationship	should be more distant relationship
Dynamic/flexible/iterative Study Design?	yes	no
Power Differential Perception of PI over Subject	can be minor or major	usually major
Risk of Physical Harms (e.g. illness, death, etc.)?	no (though yes rarely)	yes
Risk of Social Harms (e.g., embarrassment, employability, etc.)?	yes	yes
Generalizable to other settings/populations?	can be yes or no	yes
Requires IREC review?	can be yes or no	yes

WORDS TO LEARN

As a new IREC member, you will come across terminology you may not be familiar with. Don't worry; this is common for anybody who is new to IREC. The list below includes definitions/descriptions of some of the common terms used in human subjects research. This section on terminology provides:

1. Project review terms
2. Study related personnel terms
3. IREC related personnel terms
4. Research related statistics terms

PROJECT REVIEW TERMS

Amendments – These are changes to an IREC approved research protocol and must be submitted and approved by the IREC before implementation (e.g. revised consent document, change in personnel, additional risks). Amendments involving more than minor changes or changes that pose more than minimal risk will be reviewed by the full committee.

Coded Data – Replacing identifiable data/private information (e.g., name) with a 'code' (e.g., letters, symbols or numbers). The goal is to protect the identity of the subject. The key is that the code is not kept with the data.

Common Rule – United States federal rules and regulations that IRECs must adhere to were codified in 1991 Policy for the Protection of Human Subjects (45 CFR 46).

Confidentiality – Describes the protections taken to safeguard data/information obtained from a subject.

Continuing Review – Periodic re-review of a research study by IREC to evaluate if risks to participants remain reasonable in relation to potential benefits, and to evaluate if the study continues to meets regulatory and institutional requirements.

Deception – Deception is the intentional misleading of subjects or intentional withholding of information about the nature of a study. Deception limits the ability of subjects to provide truly 'informed consent'; however, it is sometimes necessary for certain types of behavioral research. Deception is often justified because humans act differently depending on study circumstances, and full disclosure of study information/goals may bias the results.

De-identified Data – Data is considered de-identified when unique identifiable information (e.g., name, address, etc.) is removed from the data so that the subjects/source cannot be identified.

Exempt Research – Certain kinds of research involving minimal or less than minimal risk may be "exempt" from IREC oversight when the activities fall into one or more of the exempt categories.

Expedited Review – Regulations allow for an expedited review (one reviewer only) for certain kinds of research involving no more than minimal risk. For a list of the expedited research categories, click here. IREC Chairs and other experienced/trained IREC members designated by the IREC chair may conduct expedited reviews.

Full Board Review – Research involving greater than minimal risk must be reviewed at a fully convened meeting, where a majority of the committee members are present.

Human Subject – Under the federal regulations, 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.

Human Subjects Training Certification – Human subjects training certification is required for research approval at many institutions, including NU. NU uses an online educational program called CITI Human Subjects Research.

Informed Consent – A person's voluntary agreement to participate in research, once they've understood the possible risks and benefits of participation. Consent may be written or oral in defined circumstances, or translated from a language other than English.

Minimal Risk – A risk is minimal when the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in the participant's daily life or during the performance of routine physical or psychological examinations or tests.

Multi-site research – A research study conducted at more than one institution (nationally and/or internationally) using the same protocol, each with its own Principal Investigator. Many clinical trials involving drugs/devices/biologics are conducted at more than one site.

Privacy – Privacy refers to the subject and his/her control over the extent, timing and circumstances of sharing oneself (physically, emotionally, behaviorally, or intellectually) with others.

Protocol – The formal design of an experiment or research activity. The protocol includes a description of the research methodology, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data. Research involving drugs, devices, or biologics will have a formal clinical protocol, which is submitted with an IREC application. For non-clinical social and/or behavioral research, a properly completed IREC application can serve as the protocol.

Reportable Events – At NU, the term "reportable events" refers to: adverse events, unanticipated problems involving risk to subjects or others, protocol violations, and data safety monitoring reports. Reportable events are submitted to the IREC in a reportable events form.

Research – Regulations define research as "a systematic investigation, including development, testing, and evaluation, designed to develop or contribute to generalizable knowledge" (45 CFR 46.102(d)). Research is usually described in a formal protocol that sets forth an objective and a set of procedures to reach that objective.

Sponsored/funded research – Sponsored or funded research is research that is financially supported by an outside entity. The funding may come from a pharmaceutical company, from a foundation, a donor, or the government.

Study Sample – The number of subjects the investigator wishes to enroll in a particular study. This number can change, depending on the stage and goal of the study. For example, a pilot study may have 5 subjects, and a Phase III clinical trial may have 500 subjects. A social and behavioral study could have a whole tribe or selected individuals. Target accrual must be justified in IREC applications.

STUDY RELATED PERSONNEL TERMS

Co-Principal Investigator (Co-PI) – In addition to the principal investigator, the co-principal investigator is the scientist or scholar who shares responsibility for the design and conduct of a research project. The Co-PI may be involved with a large portion of the research, or a small portion. The type and amount of study involvement depends on the responsibilities agreed upon by the PI and the Co-PI.

Data Manager – An individual who handles the data gathered during a study. Responsibilities may also involve managing data entry, database generation and/or maintenance, compliance with regulations, and protection and integrity of private information and study data.

Faculty Advisor – Faculty advisors are faculty members who supervise and oversee research being conducted by students. Advisors are responsible for guiding students through the IREC process, helping with research design, methodology, and ethical considerations.

Principal Investigator (PI) – The lead scientist or scholar who holds the ultimate responsibility for the conduct of a research project. The PI is the signatory authority of the study.

IREC RELATED PERSONNEL TERMS

IREC Chair – The role of IREC chairs vary by institution, but commonly IREC chairs direct the proceedings of IREC meetings. IREC chairs also review and approve research qualifying for expedited and exempt review. Furthermore, the IREC chair plays a leadership role in creating IREC policies and procedures.

IREC Secretary – An administrative staff person, who is responsible for screening and reviewing IREC applications prior to committee review. This job also includes agenda preparation, taking minutes and drafting correspondence between the PI and IREC.

IREC Vice-Chair – The role of the Vice-Chair is to fulfill the IREC Chairs responsibilities when the Chair is unavailable. Vice-Chairs also may review and approve research qualifying for expedited and exempt review.