

**American University of Beirut
Faculty of Medicine
Institutional Review Board**

Principles and Procedures

Original Version dated May 2001
Last Revised Version (# 5) dated February 2007

Table of Contents

- I. Introduction**
- II. Ethical Principles Guiding the Work of the IRB**
- III. Functions and Operations of the IRB**
- IV. Schedule of IRB Meetings**
- V. What is to be reviewed by the IRB?**
- VI. Submission of Proposals**
- VII. Special Circumstances**
- VIII. IRB Review of Research Proposals**
- IX. Responsibilities of the Principal Investigator (PI)**
- X. Questions and Appeals**
- XI. Ongoing Reviews and Extension Requests**
- XII. Modification of Proposals**
- XIII. Project Closure**
- XIV. Protocol Deviations/Violations and Incompliance Incidents**
- XV. Termination/Suspension of Research**
- XVI. Monitoring of Approved Proposals**
- XVII. Records and Documents**

Appendices

- [Appendix 1. Flow Chart – IRB Review and Approval process](#)
- [Appendix 2. IRB membership list – October 2006](#)
- [Appendix 3. Guidelines for Submitting Research Proposals](#) (submission Checklist and submission forms)
- [Appendix 4. IRB Submission Form for Expedited &/or Full Review](#)
- [Appendix 5. Application form for Exempt Proposals](#) (updated 2005)
- [Appendix 6. Informed Consent Checklist](#) (updated 2005)
- [Appendix 7. Informed Consent Templates](#) (English and Arabic updated 2005)
- [Appendix 8: Genetic Informed Consent Templates](#) (English and Arabic updated 2005)
- [Appendix 9: Assent Forms Templates](#) (For Children and Adolescents New 2005)
- [Appendix 10. Forms for Funding](#)
 - [URB](#)
 - [Grants and Contracts](#) (All extramural)
 - [LNCSR](#)
 - [MPP and DTS](#)
- [Appendix 11. Investigational Drug Information Form](#) (updated 2005)
- [Appendix 12: Adverse Event Form](#) (New 2005)
- [Appendix 13. Ionizing Radiation Use Forms in Humans](#)
 - [Use of X-rays](#)
 - [Use of Unsealed Radioactive Material](#)
- [Appendix 14. Request for Continuing Review and Re-approval \(Progress Report\)](#) (updated 2005)
- [Appendix 15. Glossary: Clinical Trials Terminology](#)

I. Introduction

The Institutional Review Board (IRB) is an administrative body established to protect the rights, safety and well-being of all human subjects recruited to participate in research activities conducted by members of the Faculty of Medicine and Medical Center, American University of Beirut (AUBFM/MC), or on the premises, regardless of the funding source. In addition, the IRB pays special attention to studies that may include vulnerable subjects. All research involving human subjects conducted at the AUBFM/MC must be reviewed by the IRB except for those deemed exempt from such review (see section VI).

The committee is composed of at least 5 members, one of whom must have primary concerns in nonscientific areas, and one must be not affiliated with the institution and is familiar with the community's attitudes and sensitive to its issues. The chair of the IRB is the dean of the faculty of medicine or his/her representative. The members will collectively have the qualifications and experience to review and evaluate the science, medical aspects and ethics of the research proposals (refer to Appendix 2 for current membership list).

The IRB can approve, request modifications in, deny approval or terminate/suspend any prior approval to, any research activity that falls within its jurisdiction. Approval by the IRB is required for all research activities to be conducted at AUBMC or by AUBFM faculty members. However, approval does not necessarily imply that the proposal will be funded or will be executed.

The IRB works in close coordination with the Research Committee, which is responsible for reviewing the scientific merit of research proposals submitted for funding from sources within the AUB (refer to Appendix 7 for specific forms). The IRB may call on the Research Committee or on reviewers of its own choosing to aid in the scientific review of submitted proposals when needed, but makes its own independent decision regarding approval or disapproval of a research proposal based upon its primary responsibility, i.e., to ensure the welfare, safety and protection of human subjects.

For the purposes of the above, “**research**” may be defined as “a systematic investigation, including research development, testing and evaluation, which is designed (in whole or in part) to develop or contribute to generalizable knowledge”. “**Human subject**” is defined as “a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information”. “**Intervention**” includes “both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes”. “**Interaction**” includes “communication or interpersonal contact between investigator and subject”. “**Private information**” includes “information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects”(45 CFR 46. 102).

Some studies are exempt from review by the IRB. Some, which involve minimal risk to the human subject, may qualify for expedited review. Special procedures apply for submission of such requests. Some proposals will require the full review of the IRB. Other categories of review apply as well, e.g., emergency IRB approval, rapid response reviews (see section VI).

II. Ethical Principles Guiding the Work of the IRB

Several documents have explored or expressed in detail the guiding principles and the procedures to be followed by IRB's in conducting their work. These include (among others):

1. The Nuremberg Code <http://ohsr.od.nih.gov/nuremberg.php3>
2. The Belmont Report <http://ohsr.od.nih.gov/mpa/belmont.php3>
3. The Declaration of Helsinki http://www.wma.net/e/policy/17-c_e.html
4. The US NIH IRB Guidebook http://ohrp.osophs.dhhs.gov/irb/irb_guidebook.htm
5. US Code of Federal Regulations, Department of Health and Human Service; Public Welfare: Protection of Human Subjects (45CFR46) <http://ohsr.od.nih.gov/mpa/45cfr46.php3> and Food and Drug Administration: Protection of Human Subjects (21CFR50) and Regulations for IRB (21CFR56) <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm>
6. Good Clinical Practice/International Conference of Harmonization. ICH guidelines <http://www.ich.org>

This document is derived and based on all of the above.

Other bioethics related resources could be found at <http://www.aub.edu.lb/~webmedic/InternetResources.htm>

1. Basic Ethical Principles

The three main principles which guide the IRB in making its decision are derived from the Basic Ethical Principles highlighted in the Belmont Report document dated April 18, 1979. They are as follows:

- a) Respect for Persons
- b) Beneficence
- c) Justice

a) Respect for Persons

The principle of respect for persons entails two moral requirements: the acknowledgment of the autonomy of the subject and the protection of those with diminished autonomy. In other terms, the principle requires that subjects participating in the research should be fully aware of the nature of such research and assured that such participation is voluntary, with no pressure or duress. They should also be aware of the physical, psychological, and socio-economic risks that such participation might bring to the subject immediately or in the future. This requirement is imperative, even if the risks were described as minimal or insubstantial.

Further, it requires the preservation of the privacy of individuals and the confidentiality of the information about them that will be obtained during the course of the research. Certain precautions should be taken in connection with those subjects suffering from diminished autonomy, namely: minors and disabled persons. These people may need further protection, perhaps to the extent of excluding them from participation in certain research.

b) Beneficence

Beneficence here means more than kindness or charity, it requires researchers to maximize the potential benefits to the subjects and minimize the potential risks. The benefits that the other subjects

involved in such research or society at large (in the form of generalizable knowledge) will reap from such research should always outweigh the acute and long term risks to which the subjects involved in the research are exposed to.

The Hippocratic maxim “Do no harm” has long been a fundamental principle of medical ethics, requiring physicians to benefit their patients “according to their best judgment”. It is contended, however, that avoiding harm requires learning what is harmful. In the process of obtaining such knowledge, persons may be exposed to risks of harm. Similarly, learning what will in fact be beneficial may require that persons be exposed to risks.

In all, it is important to arrive at a decision as to when it would be justifiable to seek certain benefits despite the risks involved, and when benefits should be forgone because of such other risks.

In hard cases, like research involving children with the purpose of finding effective ways of treating childhood diseases, the different claims covered by the principle of beneficence may come into conflict and force difficult choices, like including children in research when those same subjects are not the direct beneficiaries of such research.

c) Justice

The principle of justice requires an equitable and fair selection of subjects and a fair and equitable distribution of risks and benefits of research. Particular attention should be directed to vulnerable persons, like children, prisoners, patients and impoverished individuals, in so far as the matter of their inclusion or exclusion from research is involved.

It is equally important that research work should not depend on easily available subjects resulting from continued social, religious or other forms of illegal discrimination; neither should it be associated with situations in which unfair pressure is placed on subordinates.

Furthermore, data extracted from subjects can be of importance to them. The principle of justice calls upon investigators to treat such data as strictly confidential. Such data is not to be taken as the investigators’ property. Indeed, it would be fair and just to see subjects more as partners in research rather than as mere vessels of data

2. Special Risk Groups or Vulnerable Subjects

Pregnant women, fetuses, children, prisoners and mentally incompetent persons are considered vulnerable subjects who may be in need of greater protection.

a) Pregnant Women and Fetuses

Some controversy exists about the inclusion of women of childbearing potential in research studies. The principle of Justice suggests that women should be included in all studies so that the research findings may be of benefit to all persons at risk of the disease or condition under study. On the other hand, use of women of childbearing age in research is discouraged because of the inherent dangers of some research procedures. Investigators should be assured that female subjects do not become pregnant during the course of research unless they are sure that no potential danger exists in such experiments. However, as to the general requirements of research by IRB, research with non-pregnant persons should form the basis of the risk/benefit assessment for fetal research.

If abortion is involved, the investigators may have no part in either the decision to abort or decisions about timing or the method to be used. No monetary or other inducements may be offered to a woman to induce her to abort (terminate pregnancy) for research purposes.

The IRB follows special regulations in order to approve research that lies under the following categories (IRB Guidebook, Chapter VI):

- *Research Directed Toward the Fetus In Utero*

Such research may involve the fetus either directly or indirectly. The research may be directed toward the pregnant woman (in which case the fetus is indirectly involved), the fetus (directly involved), or both.

For research activities directed toward pregnant woman to be approved by the IRB then the following must be satisfied: (1) the purpose of the activity is to meet the health needs of the mother, and the fetus will be placed at risk only to the minimum extent necessary to meet such needs; or (2) the risk to the fetus is minimal.

For IRB approval of research directed toward fetus in utero: (1) the purpose of activity is to meet the health needs of the fetus, or (2) the research poses no more than minimal risk to the fetus.

- *Research Involving the Fetus Ex Utero*

If an ex utero fetus is judged viable (able to sustain life independently) it is then called an infant. In this case, the IRB will be guided by regulations and policies dealing with children. A fetus is judged nonviable, unable to sustain life independently even with medical therapy and will therefore die. Ethical considerations call upon investigators to maintain the dignity of this dying human subject and to avoid intrusions in the process of dying for research purposes.

- *Research with Dead Fetuses, Fetal Material, and the Placenta*

Research activities involving the dead fetuses, fetal material, or cells, tissues or organs excised from a dead fetus are governed by Country Laws, which should be strictly adhered to and Customs/Views held by the people, which should be taken into consideration.

Consent for Research Involving Fetuses

In all research in which human fetuses are the subjects of research, the consent of the parents (mother & father) on behalf of the fetus is required. Exceptions to the requirement that the father provide consent are permitted only if: (1) the father's identity is unknown; (2) the father is not reasonably available; (3) the pregnancy resulted from rape.

In all cases, the IRB should ensure that the information provided to the parent(s) clearly distinguishes purposes of the procedures. Risks to the mother should be, so far as possible, distinguished from risks to the fetus.

b) Children and Mentally Incompetent Persons

In general, use of children under 18 years of age should be discouraged. In particular, if over 12, written consent is required, together with permission of parents or guardian (s), in certain projects with minimal risk and/or favorable risk / benefit ratio. The case should be to be submitted to the IRB for consideration and approval.

Approval may be given by IRB if there is minor increase over minimal risk, even when no direct benefits to subjects exist and the protocol is such as likely to produce general knowledge of vital importance about the child condition.

Consent & Assent of Children & Incompetent Persons

Following an evaluation on age, maturity, psychological state, the assent of the child should be sought. Parental permission analogous to informed consent is required for every research involving

children. Such permission is sufficient from one parent in projects of minimal risk; otherwise, consent of both parents is required. If one parent is deceased, incompetent or unknown, or one parent holds legal custody of the child, individual consent is acceptable. In case both parents are unavailable, intervention of the competent court is necessary to designate an official representative to look after the interests of the child. When children are involved in research, the assent (knowledgeable agreement) of the child ([download the form](#)), in addition to the permission of the parent (s) is required and should be documented. The regulations do not specify a particular age at which assent must be sought, but for most studies, the IRB suggests obtaining assent beginning at about age seven.

III. Functions and Operations of the IRB

The Institutional Review Board complies with GCP and applicable regulatory requirements. The following are the functions and operations of the Institutional Review Board (ICH/GCP section 3.2-3.3 and 21CFR56.108):

- Ascertain the acceptability of proposed research in terms of institutional commitments and regulations, accreditation requirements, applicable laws and standards of professional conduct and practice.
- Conducts initial and continuing review of research proposals to ensure compliance with international standards of ethical practice and the approved protocol.
- Determines which project requires review more often than annually.
- Ensures that changes to approved research plans are not implemented without IRB review and approval except when necessary to remove immediate significant hazard and to ensure human safety
- It is the chairperson's responsibility to review and evaluate proposals that lie under the special circumstances sections such as exempt proposals, expedited review, rapid response and emergency approval required from IRB. The members of the IRB will be notified of such decisions during the following IRB meeting.
- Recommends the suspension of an ongoing research activity in case of deviation from the protocol and existing guidelines
- Approval by a simple majority of those members present is required for the research to be approved by the IRB

IV. Schedule of IRB Meetings

Meetings are held on a monthly basis and more frequently if the need arises.

- Quorum shall consist of a simple majority of the members of the IRB
- All documents should be submitted to the Office of the Assistant Dean for Research before closing two weeks prior to the scheduled meeting date. Thus, the shortest time lag for consideration of a submitted proposal by the IRB is 2 weeks, and the longest is 6 weeks.
- For proposals requesting funding from University sources (MPP, URB, DTS etc...), other deadlines apply and are announced periodically. For such proposals, submission to the IRB will be the responsibility of the Assistant Dean for Research after review and funding recommendations by the Research Committee have been concluded.
- Proposals that qualify for expedited review or rapid response review may be submitted at any time.
- Provided the proposals are complete and are submitted before the deadline for a particular meeting date, the IRB will provide a decision during that meeting.

V. What is to be reviewed by the IRB?

Research that requires IRB review includes any research on human subjects that:

- ✚ Is conducted by AUB faculty, staff or students.
- ✚ Is performed on the premises of the university.
- ✚ Is performed with or involves the use of facilities or equipments belonging to the university.

This includes but is not limited to,

- ✚ Research projects conducted at other sites or in foreign countries by Faculty researchers should be reviewed by the IRB of these sites and by our IRB. The standards for ethical conducts should not be lowered.
- ✚ Research that is part of a multicenter clinical trial. Even if approval on a national level is secured, IRB review is needed.
- ✚ Faculty supervised student research and research conducted in courses (see special circumstances :class assignments)
- ✚ Pilot and feasibility studies (the consent must include a statement that this is a pilot study)
- ✚ Research involving the use of data of human subjects gathered in earlier projects (that can be identified or blinded)
- ✚ Research on human tissue or fluids collected originally for clinical or diagnostic purposes but no longer needed or for investigational purposes.

VI. Submission of Proposals

The principal investigator must submit 5 copies of the proposal if requesting intramural funding (MPP, DTS, URB) or 3 copies if for extramural funding or no funding along with the required signatures and coversheets to the Assistant Dean for Research, Faculty of Medicine. More copies may have to be submitted if required by the funding agency e.g. LNCSR. The documents required include all the following:

1. **Coversheets:** [IRB Submission Form](#) for research from the Faculty of Medicine and the Research Proposal Form if requesting funding from MPP, DTS, URB or the [Institutional Review Board Coversheet](#) for research from other Faculties. Please complete all other necessary forms for funding purposes e.g. [URB cover sheet](#) if requesting funding from the University Research Board, [Grants and Contracts](#) cover sheet if funding is from an outside source and [LNCSR](#) if requesting funding from the Lebanese National Council; see Appendices for required forms) (required)
2. **Cover letter** with a summary of the proposed work if the protocol is submitted by a sponsor and not written by the principal investigator, specifically indicating the number of subjects to be recruited at AUBMC and the duration of the study. Please also provide a copy of the Investigator's Signature page signed by the PI and the sponsor representative. (required)
3. **Detailed research proposal/protocol** as per guidelines of the Research Committee, unless the funding agency has special forms or requirements for that purpose. (required)
4. [Informed consent form in Arabic](#) using AUB required wording on signatures page (Appendices 6 to 9), and Letter of Information to the patient (if applicable). Or a description in the application as to why an informed consent document is not possible or appropriate for the study (check Special Circumstances VII section 5 for Waiver of informed consent forms) Please refer to Appendices 6 to 9 for [Informed consent](#) issues

5. [Application form for exemption from IRB review](#) (if applicable).
6. Information about **payments or compensation** available to subjects (if applicable)
7. **Subject recruitment methods** (e.g. advertisements, brochures, flyers, audio tapes, video tapes or letters to potential subjects) that will be used to inform people about the study (refer to section VII for minimum requirements) (if applicable)
8. Any questionnaires or surveys. Phones scripts for situations that will involve providing information to potential participants via telephone. (if applicable)
9. If an outside agency, company, hospital or clinic is giving access to its clients, files, or premises, a letter of agreement from that agency that confirms knowledge of the project's purposes and gives permission for the investigator to conduct the study there.
10. Investigational Drug Information Form (if applicable)
11. **Clinical Investigator Brochure** (CIB) and/or Product Monograph (**ONLY ONE COPY IS REQUIRED**)
12. Ionizing Radiation Safety Forms (if applicable). Two forms exist: one for use of X-rays and one for unsealed radioactive material. Research protocols which expose the human subject to ionizing radiation (radioactive materials or ionizing radiation producing machines) must include the applicable form(s). If the research proposal involves only radiation procedures received by a patient over the normal course of care (i.e. radiation received regardless of participation in the study) then no form(s) is required. Research proposals which include radiation procedures received over the normal course of care (clinical) and additional radiation received as a direct result of participation in this study, then the applicable form(s) must be filled, however, the 'clinical' procedures are not to be included.
13. **Curriculum vitae** of principal investigator and co-investigators. **(required)**
14. **Insurance certificate** from sponsor for all medical expenses incurred as a result of adverse reactions occurring to the human subject which may arise directly from participation in the study (e.g. drug reaction). **(required)**
15. **Detailed budget** **(required)**

Please refer to [Guidelines for Submitting Research Proposals](#) ([Appendix 3](#), Word format) for more details. Also note that all forms listed above can be found in the Appendix section.

VII. Special Circumstances

Listed below are special circumstances that affect the review of research by the IRB:

1. Exempt Proposals

There are several areas or types of research that, although involving human subjects are exempt from the IRB's review and approval process (Appendix 1). These are activities that do not expose human subjects to any physical, social or psychological risks. In general, these require that information needed for this research be recorded in a manner whereby the human subject concerned cannot be identified, directly or indirectly. It may be necessary to submit a study application to the IRB to ascertain that these conditions are met. The following types of research qualify for exemptions from IRB review (45CFR46.101):

1. Research involving normal educational practices such as i) research on regular and special education instructional strategies, or ii) research on the effectiveness of or comparison among instructional techniques, curricula, or classroom management methods.
2. Research involving the use of educational testing, survey procedures, interview procedures or observation of public behavior where the information obtained is recorded in such a manner that human subjects cannot be identified, directly or through identifiers linked to the subject

3. Research involving collection of existing data, documents, records or specimens collected if these sources are publicly available or subjects cannot be identified directly or indirectly.
4. Research involving taste and food quality evaluation and food acceptance.
5. Research and demonstration projects designed to evaluate public benefit or service programs

Any investigator who thinks that his/her study qualifies for exemption should discuss this first with the chairperson or members of the IRB and/or fill a special form to be submitted to the IRB along with the study proposal/protocol (see Appendix 5. [Application Form for Exempt Proposals](#))

2. Proposals Eligible for Expedited Review

Research where there is no more than minimal risk to human subjects or minor changes to previously approved research may be reviewed and approved by the chairperson of the IRB or his designee. The principal investigator should request this by filling the application form for proposal (see Appendix 11. the IRB Submission Form). The chairperson must report his decision to the IRB at its regular meeting. The general categories of research and examples where expedited review may apply are the following:

1. Collection of blood samples by finger stick, heel stick, ear stick or venipuncture. The specific guidelines for the total amount and frequency of blood withdrawal take into consideration the age, weight and health of the subjects: for adults, normally no more than 450 ml during an 8 week period, and not more than twice a week collections are allowed. For younger individuals and those < 50 kg, not more than 50 ml or 3 ml/kg whichever is less during an 8 week period is allowed.
2. Prospective collection of biological specimens for research purposes by noninvasive means. Examples include non-disfiguring hair and nail clipping, excreta and external secretion, placenta at delivery, mucosal and skin cells collected by buccal scraping or swab, skin swab or mouth washings, etc.
3. Collection of data through noninvasive means routinely employed in clinical practice excluding x-rays and microwaves. Examples include: electrocardiography, electroencephalography, magnetic resonance imaging, ultrasound, echocardiography, body composition, moderate exercise by healthy volunteers, muscular strength testing, weighing testing sensory acuity.
4. Research involving materials already collected or will be collected solely for non-research purposes, e.g., documents, records, pathological specimens, or diagnostic specimens.
5. Research on individual or groups characteristics or behavior such as perception, cognition, test development where the investigator does not manipulate that subject's behavior and no stress to the subject may occur, or research using survey, interview, oral history, or quality assurance methodologies.

3. Course-Related Student Projects:

Honors theses, and Master's or Doctoral Theses involving human subjects must be submitted for IRB review. Some student projects conducted to fulfill course requirements involve activities that might be viewed as research. Student class assignments include those conducted during or outside of class with students enrolled in an official course (for credit or not for credit), as well as activities in fulfillment of class assignments involving interactions with individuals other than the members of the class. These assignments are completed within the academic semester. Faculty members may

design assignments that engage students in interaction with individuals or fate about individuals to teach research methods or to help students understand concepts covered by the course. They are not intended to create new knowledge or to lead to scholarly publication. These types of assignments do not fall under the jurisdiction of the IRB and do not require IRB application, approval or oversight. When some assignments are being conducted with the intent to develop or contribute to generalizable knowledge, they are considered research. Some class assignments may pose little or no risk to students. These risks may include potential psychological, social, economic, or legal harm, especially when data is collected about sexual activity, use of alcohol or illegal drugs, or involvement in illegal activities. Instructors should make sure that the students realize the potential for harm when collecting information about these issues. These assignments need to be submitted to the IRB for review and approval before they begin. They might fall under the categories of “exempt” research or “Expedited” research. Faculty members should help students understand that they are obligated to minimize risks to other students or to any other people with whom they interact to complete their assignments.

4. Genetic Research:

Genetic information is personal and it has the potential to influence employment, insurance, finance, education and self perception.. Genetic information must be carefully maintained in order to protect against stigmatization, discrimination, or significant psychological harm to the subject. If minors are involved in DNA research, the parents or legal guardians must review and sign the genetic informed consent document. This will give them the option of whether or not they want the results of the genetic analysis disclosed to them. Whenever appropriate, the minors assent should be asked for. Investigators must follow the appropriate measures with regard to releasing such information. In some cases it may be possible to determine that some members of the family are not genetic relatives, Issues of genetic relationships (paternity or maternity, as could be hidden by adoption or donor fertilization) and other incidental information should not be revealed. Genetic informed consent forms are critically important (refer to the checklist and templates for more information).

5. Waiver of Informed consent form:

An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research

The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

(1) The research involves no more than minimal risk to the subjects;
(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;
(3) The research could not practicably be carried out without the waiver or alteration; and
(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

(e) The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.

However, the investigator may be required to prepare a written justification statement to the subject explaining the purpose of the study and why the consent form was waived.

6. Rapid Response IRB Review

This is specially designed to deal with those industry-sponsored protocols whereby the sponsor deadline for IRB approval is such that it cannot be considered at one of the scheduled IRB meetings. Alternatively, the sponsor may have provided the protocol at a date too late to submit to the previously scheduled IRB meeting. (See section IV). The chairperson of the IRB will determine on a case-by-case basis the eligibility for Rapid Response Review.

7. Emergency IRB approval

Physicians may be granted an emergency approval to treat a single patient on a research protocol and/or use of an investigational drug or device. To be eligible, the patient must be suffering from a serious life-threatening disease for which there is no satisfactory alternative, and there was no sufficient time to obtain regular IRB review and approval. The physician must obtain the informed consent of the patient.

The chairperson of the IRB may grant the approval orally. The physician should, however, submit a report to the IRB within 5 days of the administration of treatment describing the following:

- Name of the Subject
- Name of the Investigational Agent
- The rationale for the use of the investigative treatment and any observed outcomes (positive or negative),
- A copy of the signed informed consent form or a statement from a physician not involved with clinical investigation verifying that the situation was life threatening, necessitating the use of the agent, informed consent could not be obtained, and no alternative method of approved or generally accepted therapy was available for this patient. These documents must be submitted to the IRB.
- Approval for emergency situations are on an individual basis and each situation must be presented to the IRB

VIII. IRB Review of Research proposals

1. Recommendations and Decisions

Members of the IRB are charged with reviewing proposals requesting exemption from review, expedited or full review. In addition, they may call on experts or on the Research Committee to aid in the review process. The IRB will coordinate with the Department of Health Physics Services for all research proposals that involve the use of radiation. For proposals requiring exemption or expedited review, the members communicate their recommendations to the chairperson of the IRB directly. For those requiring full review, the members present a summary to the IRB during a scheduled committee meeting and make a recommendation for that research proposal. Recommendations fall into four categories: either to

1. Approve the project as proposed
2. Withhold approval pending minor revision of the proposal
3. Deny approval and recommend major revision of the proposal

4. Terminate or suspend a previously approved proposal

The IRB chairperson is empowered by the IRB to approve, withhold approval or deny it for proposals requesting exemption or expedited review. The chairperson may not agree with the recommendations of the reviewers and may withhold approval of a proposal pending minor or major revision.

Decision on proposals requiring full review of the IRB is usually reached by consensus. If consensus is not reached, then the IRB will resort to a vote, whereby a simple majority is required for approval.

The IRB chairperson communicates to the principle investigator the decision of the IRB in writing. If approval is granted, the principal investigator may begin work on the research as approved and for the period specified. Typically, research proposals are approved for not longer than one year. In some cases, the IRB may approve a proposal for a shorter period of time and require a progress report before extending the approval for a full year.

For approved proposals, the letter of the chairperson will, therefore, include:

- a) Name and address of the IRB
- b) Date of approval
- c) Investigator's name
- d) The title and official references or codes to the proposal
- e) A statement of approval for all documents submitted and approved such as the protocol, informed consent form, advertisement and clinical investigator brochure etc.
- f) Duration of the approval (usually not more than 1 year; may be less)
The need for a progress report and the time it is to be submitted (usually at one year but may be less)
- g) Comment regarding safety updates
- h) Note that IRB operates under the GCP/ICH guidelines, FDA and local regulations

If approval is withheld or denied, the letter must detail the IRB's concerns and reasons for withholding or denying approval, and its recommendations for revision of the proposal.

The principal investigator will submit revisions to the chairperson of the IRB and the Assistant Dean for Research within a time frame specified by the IRB chairperson's letter. The revision will be considered by the IRB chairperson (for expedited review) and by the full committee (for full review) and a decision will be made accordingly.

2. Advertisement

The IRB is responsible for reviewing methods of recruiting study subjects to assure equitable selection of subjects and protection of subject's rights. This is done to increase enrollment by the investigator. The IRB should approve the information contained in each advertisement and the medium used (e.g. newspaper, website, bulletin, TV, poster, questionnaires, etc). The IRB should assure that all information in advertisements avoid undue coercion and is not misleading to subjects. This is specifically relevant to vulnerable subjects. As a result of that, extra diligence is required to assure their right.

The advertisement should be limited to the following:

- Name and address of the clinical investigator or institution
- The purpose of the research and summary of eligibility criteria
- A description of the benefits for subjects (payment or free exam)
- Location of research
- Whom to contact for further information

The IRB is also responsible for approving outsourcing methods of recruitment such as questionnaires.

IX. Responsibilities of the Principal Investigator (PI)

a) Certification

The PI and all co-investigators, research assistants, research coordinators, students, residents, statisticians and other personnel who plan to conduct research studies involving human subjects must take and pass a web-based course entitled: **“Human Participant Protections Education for Research Teams”**, offered by the National Cancer Institute of the National Institutes of Health, USA. A signed and dated copy of a certificate, issued by the NIH upon successful completion of the course, must be submitted to the IRB Office - Office of the Assistant Dean for Research, Faculty of Medicine, attesting to that. Principal investigators are responsible for ascertaining that all personnel who plan to be involved in a particular research protocol will take the course and get certified. Research proposals submitted by non-certified researchers will not be approved by the IRB and may not be conducted at AUB or by AUB personnel.

b) Informed consent document and Informed Consent Process

The PI or one of the study coordinators must explain the informed consent process and ask the subject to read and sign an informed consent document. The PI or designated representative must review the document with the subject, answer all questions he/she may have, and ensure that the subject will exercise power of choice without intervention of outside elements and forces, coercion or any other form of pressure. The subject must be made aware of all the procedures and the potential risks and benefits associated with the study and its duration. A copy of the signed informed consent document must be filed with the investigator study file and a signed copy should be given to the subject. The PI must keep all documents, files, videotapes, etc, that contain the subject’s personal identifier under lock throughout the study period and afterwards, until said records are destroyed or transferred to the central record room of AUBMC. The duration that the records are kept is determined by the nature of the study.

Informed Consent Process

Obtaining informed consent from a potential subject reflects the principle of “respect for persons”, which guides the work of the IRB. It assures that the research subject will understand the nature of the research and can knowledgeably and voluntarily decide whether to participate or not. The investigator or designee should consider these three elements during the informed consent process:

1. **Information:** the subject must receive information about the research purpose, procedures, risks and benefits, alternative procedures (where therapy is involved), his/her ability to ask questions and to withdraw at any time from the study. The information must allow the subject, knowing that the study may not necessarily benefit him/her directly nor is it necessary for their care, to decide to participate in furthering the knowledge on the topic in question.

2. **Comprehension:** The manner and context in which the information is presented is as important as the information itself. Rapid and confused presentations, and not allowing time for consideration or questioning, may result in an un-informed decision. The information should be adapted to the subjects' capabilities. Use of scientific jargon should be avoided and simple lay-terms and short sentences are preferable. Subjects with limited comprehension may need special treatment. Here, not only should one seek the permission of other parties who are familiar with the subject and who will act in their best interest, but also the PI should respect the subject's wishes. For example, the objections of these subjects to participation should be respected; an exception may be where this refusal or objection may lead to denying the subject a therapy that is not available elsewhere.
3. **Voluntariness:** Valid consent to participate in research applies only when given voluntarily, free of coercion or undue influence (i.e. in the absence of threat of harm for not participating or promise of reward for participating). Pressure may occur when persons in positions of authority urge a course of action for people under their influence.

c) Other responsibilities:

It is the responsibility of the PI to adhere to the following:

- To promptly report to the IRB any changes in research activity during the approval period such as protocol amendments, informed consent amendments, new information that may affect adversely the safety of the subjects and the conduct of the research.
- To submit to the IRB a progress report 1 year after initial approval and yearly thereafter requesting annual review and re-approval of the research study.
- To promptly report to the IRB any deviations from or changes to the approved protocol to eliminate immediate hazards to research subjects during the study should be reported within 10days.
- To promptly report to the IRB any unexpected results, problems or serious adverse events that may arise during the study should be reported **within 10 days**. (use the Serious/Unexpected Adverse Experience Form)

X. Questions and Appeals

Researchers who have questions about issues relating to a proposal that has been reviewed by the IRB, or to research that is in the planning stage, may contact the chairperson of the IRB and request an appointment with him/her. If resolution of problems is not possible, the principle investigator may be scheduled to present his/her case before the full meeting of the IRB. The decision of the IRB will then be final.

XI. Ongoing Reviews and Extension Requests

The IRB must conduct continuing review of the research at least annually for studies scheduled for a period of more than one year and more frequently if the IRB determines it to be indicated by the degree of risk involved with the study. Other proposals, scheduled for a period of one year, may have to be extended beyond the initial approval period (one year). In such cases, the principal investigator must request a continuation review detailing the reason for extending the study and the new anticipated date of completion of the study. This may be done in a letter (with attached documents if needed) to the Chairperson of the IRB and the Assistant Dean for Research. The review of the continuation request will occur at the same level as the initial review (i.e. the chairperson is empowered to approve continuation of proposals initially reviewed and approved

under the “Exempt” or “Expedited Review” categories, and the full IRB should approve those previously reviewed and approved as under the “Full Review” category). This review may be prompted by the IRB but it is ultimately the responsibility of the principal investigator.

The IRB approval is normally granted for not more than 1 year. If the PI will request a continuing review for extension of the study beyond one year, it is his/her responsibility to submit a request for continuing review in sufficient time to permit the IRB chair or full board to review and approve the application prior to its expiration date. As a service to the PI, the IRB will send a reminder memo one month (or two months) before the project’s expiration date. **NO HUMAN SUBJECT ACTIVITY MAY TAKE PLACE AFTER THE EXPIRATION DATE.** If the investigator does not submit the progress report by time, the investigator is notified by memo that IRB approval has lapsed. This memo shall include a reminder that no **human subjects’ research may be conducted until IRB approval is obtained.** The PI must then, submit the progress report within 10 working days after the date of the lapse of approval memo. If the investigator fails to comply, the IRB send the investigator a notification of study closure. In case of external funded studies, a copy of the notifications is sent to the corresponding offices. Once the IRB closes a project, it can only be resumed if the investigator submits the project again for IRB review and approval as a new application.

Annual review and re-approval is required after 1 year from the date of initial approval. (Refer to Appendix 14. for [Request for Annual Review and Re-approval Form](#))

XII. Modification of Proposals

If the principal investigator made modifications to a previously approved proposal or protocol, he/she must request a review of the modifications proposed. The request must be submitted to the chairperson of the IRB and the Assistant Dean for Research in the form of a letter (with any supporting documents and changes to informed consent forms) detailing the reasons and justification for the modifications and/or the changes.

The chairperson of the IRB may approve requests for modification when they are minor in nature, i.e., when they do not alter the basic nature of the research. Modifications include procedural changes to the protocol, adding or removing investigators, changing the titles of the project, requesting additional subject beyond the original approved number, new funding sources, new or revised advertisements, increasing sites of sampling, changes to the informed consent forms, surveys, questionnaires and additional new items.

However, the chairperson of the IRB must notify the IRB members of such decision during the next scheduled meeting.

Major modifications will have to be reviewed at the same or higher level as the original review (i.e., expedited review by the chairperson, full review by the IRB as a whole). Decisions on modification requests fall into the same four categories as for the proposal: approve, withhold approval pending minor modifications, and deny approval with major modifications or terminate/suspend a previously approved research. The modification, if approved, will apply for the same approval period as the original proposal.

XIII: Project Closure:

When a study ends, is closed or canceled for any reason, a Project Closure Form must be filled in. This form indicates that the annual progress report is no longer needed to be submitted by the PI. If no subjects have been enrolled in a study for a period of 3 or more years, the IRB may require that the project be closed, unless the PI can submit reasons for this low rate enrollment.

A project that has stopped recruiting new subjects but in which follow up data is still being collected or analyzed-cannot be considered closed and the PI should submit a request for continuing review until all follow-up data collection is finished. Once the Project Closure Form is submitted (to be added soon in the forms section), no more data collection about any subject is allowed.

XIV. Protocol Deviations/Violations and Incompliance Incidents:

The Principal Investigator bears the ultimate responsibility for the conduct of a research project. Investigators are responsible for conducting human subjects' research in compliance with the IRB regulations and policies and procedures.

Non-compliance with regulations may be seen as **protocol deviations**. Deviations generally do not have a major impact on subject's welfare.

The most common deviations in investigator compliance include:

1. Unreported changes in the IRB approved protocol or consent documents
2. Misuse or non-use of the IRB approved informed consent documents
3. Lapse in obtaining approval for continuing review
4. Failure to obtain IRB approval prior to starting research activities
5. Failure to file protocol modifications.

Problems such as these are often caused by investigator communication difficulties with the IRB. When such instances are discovered, the IRB will act promptly to halt the research, assure remedial action regarding compliance with human subject protection requirements.

Investigators can almost always avoid protocol deviations by being aware of the IRB requirements and following the approved protocol. **If a protocol deviation does occur, an investigator must submit a protocol deviation reporting form (to be added soon to the forms section) to the IRB for review immediately upon discovery.** This form will serve as the documentation for modifying the particular protocol; investigators must await IRB approval before implementing anticipated changes or modifications.

Protocol Violations

Protocol violations emerge when there is a variance in a research study between the protocol that has been reviewed and approved by the IRB and the actual activities being performed. Reports may come from a variety of sources: participants, community members, research staff, etc. Reporting of violations will be made, in writing, to the IRB Chairman; all reports will be held in the strictest of confidence and discussed within the confines of the fact-finding committee.

Once a protocol violation is found, the IRB will analyze all information gathered regarding the protocol violation and compare it to the approved protocol. A conclusion will then be made regarding the seriousness of the violation.

In cases of *non-serious violations*, which are actions that:

1. have no substantive effect on the safety or well-being of research participants
2. do not affect the value of the data collected (meaning the violation does not confound the scientific analysis of the results)
3. do not result from willful or knowing misconduct on the part of the investigator(s)
4. do not violate any ethical principles

The IRB chairman will notify the investigator in writing what must be done (if anything) to correct the conditions that lead to the violation and what (if anything) must be communicated to the research participants. If the PI fails to respond within 30 days of notification, the study shall be determined to be out of compliance and subject accrual shall be suspended. The IRB chairman will present a summary of the violation, process, facts, and conclusions at the next scheduled convened IRB meeting.

Serious protocol violations include violations that:

1. have or pose a significant risk of substantive harm to research participants
2. cause damage to the scientific integrity of the data collected
3. result from evidence of willful or knowing misconduct on the part of the investigator
4. impact on ethical principles

If an investigator disagrees with the findings or requirements of the Committee, investigators have the right to appeal the committee's decision to the assistant dean of Research.

XV. Termination/Suspension of Research

The IRB has the authority to suspend or terminate approval of research that is not being conducted in compliance with the IRB requirements or that has been associated with unexpected serious risk factors. Suspension and termination must be reported with a statement for the reason(s) for the IRB's action to the investigator and institution officials including the chairperson of the department, Dean and/or representative and the chairperson of the Research Committee.

Depending on the nature or the seriousness of the violation, the committee may elect to direct the IRB to audit all protocols that involve the investigator in question. If the findings of the hearing committee support research misconduct, the Dean will be notified.

XVI. Monitoring of Approved Proposals

The initial review of the proposal and its approval are based on the investigator's best estimate of the risks and anticipated results, and on the IRB's judgment based on its experience. It is only after the work has begun that the true risks to the human subjects can be evaluated. The IRB is in a better position then to make a correct judgment.

The IRB, therefore, has the right to monitor certain ongoing research activities that it has approved previously, whenever it judges that the risks to human subjects can thus be better evaluated. Whether or not monitoring of a particular study should occur, and at what frequency, is usually decided at the time approval is granted, at which time the IRB sets a date for the upcoming review.

Such in-progress evaluation may lead to a decision by the IRB to suspend or modify the research. Such a decision is taken by the IRB as a whole.

Monitoring may take several forms:

1. The investigators may be required to submit periodic progress reports.
2. The chairperson or members of the IRB may meet with principal investigators and/or co-investigators.
3. Human subjects may be interviewed.
4. Research records and informed consent forms, facilities and equipment may be inspected.

In its evaluation of on-going activities, the IRB will take into consideration several points related to:

1. Whether the clinical trial is conducted in compliance with international and local regulatory requirements, ICH GCP guidelines and the protocol
2. Whether the procedures agreed upon at the beginning of the research are being followed
3. Whether any subjects have been seriously harmed,
4. Whether the IRB was informed of any serious initially unforeseen problems,
5. Whether any important new information has arisen out of the research so far or from other sources that may affect the subjects' willingness to join the study, and thus requires modifications in the informed consent form
6. Whether special precautions should be introduced or alternatively, special requirements be relaxed, in view of the preliminary results of the study or of the results of other research
7. Whether informed consent has been obtained and whether the concerned subjects have been informed of all aspects of the study and their involvement in research.
8. Verify whether all biological samples are being appropriately collected, labeled and stored.

At the end of the review, the IRB will decide on whether the research should be continued, suspended or terminated. It will also decide on the date for the next assessment if needed.

XVII. Records and Documents

The IRB maintains adequate documentation of all IRB activities including the following (21CFR56.115):

- Copies of all research proposals submitted and accompanying documents
- Scientific review and evaluation, if applicable
- IRB meeting agendas and minutes of meetings
- Copies of all correspondence between the IRB and the investigator
- IRB membership list

Every PI is required to maintain records of all correspondence related to the use of human subjects in research. Copies of the application form, notices of approval, and signed informed consent forms must be maintained in the investigator's records. All records are subject to inspection by the IRB, auditors for study sponsors, and possibly governmental agencies.

These records will be retained for at least 3 years after completion of research.