

University of Puerto Rico
Medical Sciences Campus
Human Research Subjects Protection Office



Policies and Procedures

Institutional Review Board (IRB)

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Introduction

The University of Puerto Rico Medical Sciences Campus acknowledges that it bears full responsibility for the performance of all research involving human subjects, including complying with Federal and local laws as they may relate to such research.

The Institution will ensure that, unless specifically exempted, all research will be reviewed and approved by the IRB. The involvement of human subjects in research covered by this policy will not be permitted until the IRB has reviewed and approved the research protocol ensuring that an informed consent is required and obtained in accord with and to the extent required by the Code of Federal Regulations (CFR). When applicable, certification of the IRB's review and approval for all federally funded research involving human subjects will be submitted to the awarding agency with the application of proposal for funding or as soon as approved by the IRB. Furthermore, the IRB's review of research on a continuing basis will be conducted at appropriate intervals but not less than once per year. None federally funded research involving human subjects will be handled in the same manner.

It is the policy of this Institution, that unless informed consent has been specifically waived by the IRB, no research investigator shall involve any human being as a subject in research unless the research investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative.


The Institution will require appropriate additional safeguards in research that involves: (1) fetuses, pregnant women, or human ova in vitro fertilization, (2) prisoners, (3) children, (4) the cognitively impaired, or (5) other potentially vulnerable groups. This Institution acknowledges and accepts its responsibilities for protecting the rights and welfare of human subjects in research.

This Institution is responsible for ensuring that no performance site cooperating in the conduct of research does so without Federal department or agency approval of an appropriate assurance of compliance and satisfaction of IRB certification requirements.

The Institution maintains IRB panels in accordance with all applicable regulations. These IRBs will have the responsibility and authority in the Institution, its components and affiliates to review, approve, disapprove or require changes in appropriate research activities for the protection of human subjects.

This Institution encourages and promotes constructive communication among the IRB, research investigators, research administrators, department heads, clinical care staff, other Institutional officials, and human subjects as a means of maintaining a high level of awareness regarding the safeguarding of the rights and welfare of the subjects.

It will exercise appropriate administrative overview to ensure that its practices and procedures designed for the protection of the rights and welfare of human subjects are being effectively applied and are in compliance with the established requirements.

	University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office	Effective: 9/1/2008
	OPERATING PROCEDURES	Rev.
<p>Scope of Authority</p>		

Purpose:

To describe the authority of the IRB as defined by the Code of Federal Regulations and designated by the Chancellor of the Medical Sciences Campus.

Sources:

45 CFR 46; 21 CFR 50; 21 CFR 56

Applicability:

UPR MSC faculty, staff, students and all other affiliated investigators.

Background:

As per Institutional Assurance, the IRB shall review all new and continuing research that fall within the University of Puerto Rico Medical Sciences Campus. The IRB reviews research in accordance with current Department of Health and Human Services (DHHS) and Food and Drug Administration (FDA) regulations. The main purpose of the IRB is to protect the rights and welfare of Human subjects who participate in research.

Policies:

No research involving human participants may begin until the UPR MSC IRB has granted its approval or accepted a waiver of IRB review.

All human subjects' clinical or behavioral research conducted by UPR MSC investigators, regardless of its source of financial support, must be approved by the IRB unless the IRB determines it to be exempt from their review and must comply with IRB policies and principles

Except for research in which the only involvement of humans is in one or more of the categories exempted or waived, all research involving human subjects, and all other activities which even in part involve such research, regardless of sponsorship, must be submitted to the IRB, if one or more of the following apply:

1. The research is sponsored by this Institution, or
2. The research is conducted by or under the direction of any employee or agent of this Institution (including trainees and students), in connection with his or her Institutional responsibilities, or
3. The research is conducted by or under the direction of any employee or agent of this Institution using any property or facility of this Institution, or
4. The research involves the use of this Institution's non-public information to identify or contact human research subjects or prospective subjects.

Procedure:

UPR MSC Faculty, Staff and Students

IRB review is required for all human subjects' research conducted on or off-campus by faculty, staff, students or any other affiliated investigator. An **investigator** is an individual who assumes responsibility for part or all of the actual conduct of a research study and/or the reporting of results. When a faculty or staff member serves as a consultant that is, as expert advisor only, on a non- otherwise MSC-affiliated project, MSC IRB review of the research is not required.

Students proposing to engage in human subject research must have a faculty member as an advisor under whose supervision the research will be conducted. The student cannot be the principal investigator. In such cases the role will be responsibility of his faculty advisor or other faculty member associated with the study, while the student can be listed as co-investigator or sub-investigator.

Please note that when an employee of any type (faculty or staff, full time or part time, permanent or temporary), or a student conducts research at an institution that has its own IRB, approval is necessary **both** from the IRB at the site of the study and from the UPR MSC IRB.

UPR MSC Clinical Staff

Research conducted by clinical faculty (including *ad-honorem*) is subject to review by the UPR MSC IRB if the research is within the course and scope of their University

duties or is conducted at any of the UPR MSC- affiliated institutions, or conducted with UPR MSC databases, trainees or students.


Private physicians, who have clinical or adjunct faculty appointments, often perform important ancillary roles in research sponsored by the UPR MSC, such as: recruitment and preliminary screening of patients, follow-up of patients, adjustment of medications, performance of tests, and collection of blood/urine samples. In cases where a UPR MSC faculty member serves as the principal or a co- investigator in the conduct of the research, UPR MSC IRB will review the protocol in the standard manner. In the case when the primary responsibility is to be assumed by the clinical or adjunct faculty member for the conduct of a study at his or her private office, or at a non-affiliated hospital or facility, the research **may** be reviewed by the UPR MSC IRB if all of the following conditions are met:

1. The department chair certifies that:
 - a. the clinical faculty member is an active participant in the University's programs;
 - b. the clinical faculty member has agreed to conform to all department and university policies governing research including review and approval by the IRB of the proposed research; and
 - c. the standards of the private office or other facility where the research is to be conducted are sufficient to assure that adequate facilities and expert professional care are available for a subject in the event of difficulties;
2. Approval of the IRB (or administration if there is no IRB) of the institution where the research is to be conducted is documented,
3. The investigator understands his or her responsibilities relating to the conduct of human research and agrees in writing to abide by all requirements imposed by the UPR MSC IRB

Non Employees

Individuals who are not employees of the institutions regularly covered by the UPR MSC IRBs, but who wish to conduct research involving patients, staff, students or facilities of any of the institutions regularly covered by the MSC IRBs, must have their proposed research reviewed by the appropriate MSC IRB, must obtain MSC IRB approval before beginning the study and must submit a "Non-affiliated Investigator's Agreement together with a copy of his/her Curriculum Vitae.

These two documents are also required for those individuals who are not employees of the institutions regularly covered by the MSC IRBs and wish to serve in the capacity of a co-investigator on a research study for which the principal investigator is affiliated.

	University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office	Effective: 9/1/2008
	OPERATING PROCEDURES	Rev.
Designation of the Institutional Review Board		

Purpose:

To define the composition, membership, appointment and responsibilities of the Institutional Review Board.

Source:

45 CFR 46.107, 109 and 113
 21 CFR 50.50
 21 CFR 56.107, 109 and 113

Applicability:

University of Puerto Rico Medical Sciences Campus

Background:

As per federal regulations, each IRB shall have at least five members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members and the diversity of the members, including consideration of race, gender, cultural backgrounds, and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review the specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas.

Policy:

The IRB shall at all times be sufficiently qualified through the professional competence, expertise and diversity of its membership to ensure that a thorough and competent review is undertaken.

Procedure:

Composition of the IRB

There are currently three IRB panels at UPR MSC. They are comprised of members with varying backgrounds of expertise, experience, and diversity to promote complete and adequate review of research activities commonly conducted by the institution and to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice.

a. Diversity of Membership

The IRB membership is monitored to assure diversity of its members, including representation by varying professions and ethnic backgrounds, both genders, individuals knowledgeable about community attitudes and subject populations and individuals knowledgeable about and experienced working with vulnerable subjects (as defined in the Subparts B, C and D).

Each IRB is composed of members drawn from the following communities:

- Faculty members of the UPR MSC.
- Representatives of Different Schools of the UPR MSC (Medicine, Pharmacy, Nursing, Public Health, etc).
- Representatives of the community.
- Behavioral scientist(s).
- Prisoner's advocate.
- The Director of the Office for the Protection of Human Research Participants and/or IRB administrator (*ex-officio*, non-voting).

Voting members may have an alternate or alternates. The voting and alternate status of IRB members must be appropriate to their representative capacity and qualifications. Alternates will be nominated and appointed in the same manner as voting members, and provided the same educational materials and training as regular members. Alternates serve the same appointment period as their full Board member partner. Alternate members, and their primaries, are listed on the IRB's membership roster.

For confidentiality reasons the Office of Human Research Participants (OPPHI) will not provide or publish the names of the members of the IRB except to Federal regulatory agencies requiring specific disclosure. Others, such as industry sponsors, may request a list of IRB members identified by initials, area of specialization, and gender.

Selection and appointment

The UPR MSC Chancellor appoints all the members of the IRB. The Director of the Human Research Subject's Protection Office, in consultation with the IRB Chairs and IRB members, recommends candidates

The Chairpersons and Vice Chairpersons are chosen from Board members that have served for at least one year on a Board. The chairpersons are designated by the Chancellor while the Vice Chairpersons are selected by vote at convened meeting. The IRB members are appointed for a period of three years and . Chairpersons are appointed for five years.

Faculty members designated to the IRB need to have a professional degree (MD, PhD, RN, MSN, MSW, RD, etc.); be knowledgeable in the area they represent, and be familiar with clinical research.

Non-affiliated members are selected from the community by nomination. They are interviewed by the IRB staff to inform them about the obligations of being a Board member and to determine suitability for Board membership.

Prior to appointment as a voting member or alternate, candidates must attend an individual orientation and at least two meetings where an experienced IRB member is assigned as a mentor to familiarize them with the meeting process. A letter of appointment from the Chancellor will be sent to the appointee and a

Authority, Duties and Responsibilities

The UPR MSC IRB has the authority to review, approve, disapprove or require changes in research or related activities involving human subjects. The IRB has the authority to:

- Review and approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy.(45 CFR 46.109, and 21 CFR 56. 109)
- Require that information given to subjects as part of informed consent is in accordance with 45 CFR 46.116 and 21 CFR 50.25.

- Require documentation of informed consent or waive documentation in accordance with 45 CFR 46.117 and 21 CFR 56.109(c).
- Notify investigators in writing of its decision to approve or disapprove the proposed research activity, or of modification required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it will include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in writing, or in special circumstances, in person.
- Conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year.
- Have authority to observe or have a third-party observe the consent process and to review the research documentation.
- Review research (45 CFR 46.403) or clinical investigations (21 CFR 50.50) involving children as subjects and approve only those clinical investigations that satisfy the criteria and conditions as described in subparts D of the federal regulations cited.
- The IRB also has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with serious harm to subjects (45 CFR 46.113) (21 CFR 56.113) . Any suspension or termination of approval will include a statement of the reasons for the IRB's action and will be reported promptly to the investigator, appropriate institutional officials, and the Department or agency head.

The IRB does not have the authority to grant retroactive approval should a research study be initiated without prior IRB review.

Responsibilities of members include serving as primary reviewer for assigned protocols, reviewing assigned materials in advance of scheduled meetings, and, presenting their review at the IRB Meeting for which the project was assigned which includes assessment of risk level, recommended action and recommended period of approval. Members who do not adequately fulfill their responsibilities, as determined by the IRB Chair, may be asked to step down from IRB membership by the UPR MSC Chancellor.

Attendance Requirement

Members of the IRB are expected to attend all scheduled meetings of their IRB panel and participate in the discussion and review of all protocols. Members of the IRB who are not able to attend a scheduled meeting of the IRB should provide sufficient advance notice (at least five working days) to the OPPHI. If a member is absent for three times without the required advance notice and

justification, he or she will be asked to leave the position and a replacement will be appointed

Removal of IRB Members

IRB members, including the chair of the IRB, are subject to removal before the completion of their approved term for cause, at the discretion of the appropriate Institutional Official. They are subject to removal based on any of the following:

- a. Scientific misconduct: fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting or reporting research;
- b. Any breach of confidentiality;
- c. Failure to protect the rights of human research participants;
- d. Failure to comply with attendance requirements.
- e. Failure to report or disclose a major conflict of Interest.
- f. Failure to comply with federal regulations, institutional policies, or IRB requirements for their own ongoing research activities.

Removal of the IRB member shall be recommended by the IRB chairperson with approval of the Chancellor. Removal of the Chairperson shall be recommended by the Director of the IRB Office with approval of the Chancellor.

IRB Members Roster

OPPHI Staff are responsible for preparing, registering and updating a list of IRB members identified by name, earned degrees and representative capacity. They will also keep a file with documents to show indications of experience such as board certifications, licenses, CV etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations and any employment or other relationship between each member and the institution.

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev. 09/13/11
<p>External Institutional Review Board – Western IRB</p>		

Purpose:

To recognize the establishment of an external IRB as alternative for industry sponsored or externally funded protocols conducted at the UPR MSC.

Sources:

WIRB Services Agreement Document

Applicability:

Investigators with Industry Sponsored or externally funded Protocols

Background:

On September 15, 2005, Western IRB (WIRB®) was been established as an affiliate MSC IRB. MSC IRB is required by its policies and by the Federal Wide Assurance, to review and maintain files on all clinical research conducted within the institution. This includes the industry-sponsored protocols that are reviewed by Western IRB per contract between the institution and Western IRB.

Policies:

The University of Puerto Rico Medical Sciences Campus has affiliation with the Western Institutional Review Board (WIRB) as an alternative for the review and oversight of externally funded projects conducted at the UPR MSC.

The MSC IRB has the right to decide to keep any new research protocol at the UPR MSC for review by the internal IRB.

No other commercial IRB review will be allowed for these projects. Projects previously approved by the UPR MSC IRB's will NOT be transferred to WIRB.

Procedures:

Principal Investigators will determine whether they want to submit the research protocols to Western IRB or to the IRB of the University of Puerto Rico Medical Sciences Campus.

All industry-sponsored protocols that will be submitted to the Western IRB, should initially be submitted to the Western IRB Liaison (MSC IRB Office, Cardiovascular Hospital - Eight Floor Office 819-821) prior to its submission to WIRB.

The Initial Submission documents will include MSC IRB-specific needs to meet institutional requirements and to provide the MSC IRB with all the information needed for our files. Information on required documents is available at IRB website (irbrcm.rcm.upr.edu).

The Western IRB Liaison will retain copies of necessary documents and then will provide a letter of authorization to the Principal Investigator to submit the Initial Submission documents to Western IRB for full board review.

After this Initial Submission to the MSC IRB, all other correspondence, including renewals, amendments, and adverse events, will be sent directly to Western IRB by the Principal Investigator. MSC IRB will maintain its files by receiving copies of approvals directly from Western IRB.


The MSC IRB charges a one-time fee of \$650.00 for the processing of industry-sponsored protocols submitted to the Western IRB for review. This fee provides funds to the MSC IRB to assist in the costs associated with review. The MSC IRB uses the fee to pay for the staff time involved in the pre-review of the protocol for institutional and WIRB requirements. The fee also covers the maintenance and update of the file throughout the life of the protocol at MSC.

Studies may be submitted to WIRB® only if they meet ALL of the following conditions:

- a. The trial is externally or industry-sponsored, industry-written; FDA regulated and meets the definition of a clinical trial "A controlled study involving human subjects, designed to evaluate prospectively the safety and effectiveness of new drugs or devices or of behavioral interventions".
- b. The investigator has not previously submitted the clinical trial to another MSC IRB.
- c. The proposed research does not involve gene transfer or embryonic stem cell Research.

d. The individual responsible for the conduct of the study (the PI) must be an MSC faculty member or a MSC associated member. MSC students are not allowed to submit research projects to WIRB even if it meets the above conditions.

The UPR MSC may decide to retain a protocol for the internal IRB review if the protocol has significant local context issues such as a unique vulnerable population, involves an investigative team that has had previous serious and/or continuing noncompliance issues, or if the research design or intervention adds unusual risk for the subjects.

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev. 6 /2009
<p style="text-align: center;">IRB Administrative Office (OPPHI)</p>		

Purpose

To define the scope of authority and duties of the Human Research Subjects Protection Office of the UPR MSC.

Source

Federal wide Assurance signed with the DHHS (FWA #00005561).

45CFR 46.115
21 CFR 56.115

Applicability

This policy applies to all human subjects' research activities conducted by any UPR MSC faculty, staff, students, other affiliated investigators, or otherwise conducted at or sponsored by the University of Puerto Rico Medical Sciences Campus, irrespective of the scope, funding, or location of the research.

Background

The Office of Human Research Protection (OHRP) is the key federal office responsible for implementation of the Common Rule (45 CFR 46) and other federal regulations concerning human research protections. The University of Puerto Rico Medical Sciences Campus filed Institutional Assurance (FWA #00005561), committing to comply with federal regulations for human research subjects' protection irrespective of the source of funding.

The Human Research Subjects Protection Office, (Spanish acronym OPPHI), of the UPR Medical Sciences Campus, was created in October 2006 as the

administrative support office for the IRB. For the purpose of this document, OPPHI and IRB office will be used interchangeably

Policy

The Human Research Subjects Protection Office of the UPR MSC (OPPHI by Spanish acronym) or IRB Office, while performing administrative functions for the IRB, supports IRB responsibility to promote and enhance the ethical conduct of research; provide oversight for ongoing human subjects research; promote education for investigators, institutional officials and IRB members; and to evaluate research conduct that does not comply with the requirements of the institution.

Procedure

The IRB office is the central point of contact for investigators, research subjects, and regulatory agencies. It is responsible for organizing and documenting the IRB review process, monitoring research regulations, producing educational programs and materials for faculty and staff, and providing assurance that the MSC is in compliance with federal, state, and campus policies. The IRB Office responds to the Chancellor's Office who is the federally authorized institutional official charged with overseeing human subjects' research and IRB functions at the UPR MSC.

Responsibilities of the IRB office include:

1. Establish and administer institutional policies regarding responsible conduct of research.
2. Ensure respect, beneficence, and justice for all research participants as a result of oversight by the Institutional Review Boards (IRB) through:
 - a. Initial review of all human subjects research with approval when appropriate,
 - b. Periodic continuing review of all ongoing human subjects research protocols,
 - c. Evaluation of adverse and serious event reports,
 - d. Investigation of allegations of research improprieties and non-compliance regarding IRB policies, federal regulations applicable to human subjects research and the institutions' FWA with OHRP.
3. Serve as a resource for investigators regarding policies and regulatory requirements.
4. Serve as the liaison with the Office for Human Research Protections and the Food and Drug Administration in the Department of Health and


Human Services, as well as with other Federal departments and agencies with similar responsibilities.

5. Participate in the education and training of investigators, signatory officials and IRB members.
6. Collaborate with other area IRBs and research review committees.
7. Maintain communication with appropriate committees necessary for research involving animals, biosafety and radiation.

Other activities of the IRB Office are:

1. Receive from the investigators all research protocols and reports.
2. Verify that all required documents have been received. If any are missing, contact the Principal Investigator. Verify the completeness of the documents.
3. Serve as a communication link between the IRB members and the investigators.
4. The IRB office will create the IRB Wise accounts and maintain a register of all the investigators.
5. Assign a protocol number in the IRB Wise System.
6. Complete preliminary review process within 1-2 weeks of time of receipt of protocol.
7. Coordinate and prepare IRB meetings with adequate documentation of quorum and meeting minutes according to 45 CFR 46.115(a)(2): "show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of issues and their resolution.
8. Provide administrative assistance to the IRB.
9. The IRB office will collaborate with the IRB chair for the assignment of a primary reviewer and will indicate assignment on the corresponding meeting agenda.
10. Distribute review materials to the IRB members one week prior to the meeting.
11. Insert into the agenda all studies that have been approved by expedited review.
12. Insert approval date into database upon approval by IRB.
13. Maintain all IRB records and research files in a confidential manner and according to 45 CFR 46.115, including copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects; records of continuing review activities; copies of all correspondence between the IRB and the investigators.

14. Maintain minutes of IRB meetings in sufficient detail to show attendance at the meetings; action taken by the IRB; the vote of these actions including the number of members voting for, against and abstaining; the basis for requiring changes in or disapproving research; and a summary of the discussion of issues and their resolution.
15. Maintain a list of IRB members identified by name and representative capacity and a file of their credentials.

	University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office	Effective: 9/1/2008
		Rev.
IRB Executive Committee		

Purpose:

To define the composition, duties and responsibilities of the IRB Executive Committee of the Human Research Subjects Protection Office of the UPR MSC.

Source: Human Research Subjects Protection Office of the UPR MSC.

Policy:

The IRB Executive Committee serves as forum for the discussion and review of IRB policies and procedures, emergency situations and major operational issues related to the operation of the IRB at the UPR Medical Sciences Campus.

Procedure:


Members:

1. Human Research Subjects Protection Office's (OPPHI) director
2. IRB chairs
3. IRB administrator or other guests may be invited at discretion of the Committee.

Meetings and voting:

The IRB Executive Committee meets to bi-monthly.. Under special circumstances, at the discretion of the OPPHI director, extraordinary meetings may be called. The agenda and meeting materials will be distributed prior to the meetings. A member of the administrative staff of the OPPHI will provide staff support and coordination for the activities of the committee.

Although the OPPHI director can request a formal vote from the IRB Executive Committee, most issues are resolved by consensus.

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev.
<p style="text-align: center;">Materials Required for IRB Submission</p>		

Purpose:

To define the IRB submission requirements.

Sources:

45 CFR 46
21 CFR 56

Applicability:

Investigators, Students, IRB Members and Staff

Background:

UPR MSC utilizes an electronic system for IRB submission. The protocol review application was developed taking into consideration federally mandated criteria as well as local institutional policies and practices. The application requires that investigators respond to questions and issues that are pertinent to evaluate the significance of the research and making a risk/benefit determination. It also includes the opportunity to address institution-specific requirements.

Policy:

The development of a comprehensive protocol review application by an investigator is essential. Investigators must carefully review IRB submission requirements. Incomplete applications will not be accepted for IRB review.

Procedure:

Applications to conduct research activities, which involve human participants, must be filed with Human Research Subjects Protection Office and must be approved by IRB prior to initiation of any research activity. Materials required for submission include:

Completed IRBWISE electronic application:

This application has been designed to meet the needs of the researchers that utilize the UPR MSC's IRB. **All items in this application must be answered.** Please read each question carefully, if the question does not apply to your research answer "NO" or "N/A" as appropriate. Please do not use cross references such as "Refer to Protocol" or "Refer to Informed Consent Document." Applications, containing incomplete answers or blanks will be returned to the Principal Investigator. This could ultimately delay the review of your protocol.

Please make sure to use the appropriate application for the specific activity you want to submit (initial review, continuing review, amendment, etc).

Electronic signatures are required:

1. Signature of the investigator (PI) in the IRBWISE endorsement section, who ensures accuracy of the information contained within the submitted materials, and, upon approval, assures compliance with all aspects of the section titled "Endorsement".
2. If the investigator is a faculty member, the signature of the Department Chair warrants that he/she is aware that the Principal Investigator intends to conduct the proposed research in his/her department. If the Division Chief is unavailable, a deputy or acting chief may electronically sign the application.
3. If the investigator is a student or medicine resident, must have the signature of the faculty advisor and the Department Director , who assume **complete responsibility** for the student's research including ensuring accuracy of the information contained within the submitted materials and assuring compliance with all aspects of Section entitled "Endorsement".

Attachments:

If applicable, the following documents should be attached in the IRBWISE system: (Not all research studies will need all of these elements)

1. Research proposal/protocol (required for all studies)
2. Data Collection Forms –
You will need to attach questionnaires, surveys, medical history forms, demographic forms, phone screens, etc. and copies of data collection forms(s) to the Application. Questionnaires that will be administered via telephone interview will require submission of the interviewer's text.
3. If surveys are being used, a cover letter to the participant is required and a Copy of the survey and cover letter must be attached to the application. The cover letter must contain the following:
 - a. Explanation of why the research is being conducted (i.e. fulfillment of master degree's thesis, dissertation, etc.);
 - b. The purpose of the study;
 - c. A statement that the subject's responses will be kept anonymous or confidential and that they do not have to answer all of the questions;
 - d. If participants will be students, then include a statement that class standing or grades will not be affected by refusal to participate or withdrawal from the study; and
 - e. A statement that participation is voluntary.
- 4 Data and safety monitoring plan (for studies with more than minimal risk that are not monitored by a DSMB).

Consent and Assent Forms

(Refer to templates at irbrcm.rec.upr.edu)


Approval by other regulatory committees or other institutions' IRB

If a proposed project involves a component of research that falls under the jurisdiction of the Animal Care and Use and/or the Biosafety Offices, approval must be obtained from the appropriate Compliance Office(s) prior to review by the Human Research Subjects Protection Office/IRB.

If applicable include evidence of IRB approval of other IRB that might have jurisdiction in the research.

Supplemental Materials:

- 1 If access to research subjects is gained through other institutions, those institutions must be identified on the IRBWISE application and an authorization letter or IRB approval must be provided.
- 2 All advertisements related to recruitment (i.e., newspaper, radio, flyers, etc.) to be used.
- 3 Interview or focus group protocols, scales, all the instruments to be used for the research must be attached electronically to the IRBWISE application, e.g. complete research proposal.
- 4 When the research involves a new drug or device, a copy of the investigators brochure and IND should also be included.

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev. 3/25/09
Informed Consent and Child Assent		

Purpose:

To define the requirements for documentation of informed consent on human subject's research under UPR Medical Sciences Campus IRB jurisdiction.

Source:

45 CFR 46.116 and 117
45 CFR 46.408
21 CFR 50 Sub-part D

Applicability:

Research Investigators

Policy:

No investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representatives. Exceptions must be approved by the IRB.

It is a requirement that the investigator propose an assent plan as part of a research protocol that includes children as subjects. If the investigator believes that assent is not appropriate for children over the age of six, a waiver must be specifically requested, described, and justified in the protocol and subsequently approved by the IRB.

Procedures:

The consent process involves explaining a study to the prospective subject, ensuring that the individual has understood the information, giving that person adequate opportunity to consider all options, responding to their questions, and obtaining the individual's voluntary consent to participate. To be effective, the consent process must provide an opportunity for the investigator (or designee) and the individual to exchange information and ask questions--both at the time of recruitment and throughout that person's participation. It may involve the use of charts, models, video tapes and other audio visuals that may assist in communicating the procedures and processes that will be part of the study. For complex protocols, incorporation of diagrams and flow charts into the consent document itself is encouraged to improve the clarity and description of the research procedures and possible treatment assignments.

The consent document is a legal document containing sufficient information to allow the prospective research subject to make an informed decision about whether or not to participate in the research and ensures that adequate information is given to the subject in the process of obtaining consent. It is not intended to be a protection for the investigator and does not constitute any waiver of liability. The signed consent document provides documentation of a subject's consent to participate in a study.

The IRB must approve all consent documents to be used. Approval must also be obtained from the IRB for each modification made in the form thereafter, before instituting the change. The version of the consent document being used should match exactly with the version given final IRB approval in the protocol file. The IRB will stamp and date each approved version of the consent document. The investigators are encouraged to use the stamped and dated copies to assist them in assuring the appropriate version is in use. Guidelines for preparing a consent document follow.

Required Elements

Each of the following points must be covered in the consent document, except in cases where the point is irrelevant to the research:

1. A statement that the study involves research, an explanation of the purpose of the research and why the subject is asked to take part.
2. A description of procedures and identification of any procedures which are experimental. For example, the description of procedures should include the length and frequency of hospitalizations; number, frequency, and length of clinic visits; the total amount of time a subject should expect to devote to the study; names and types of medication; types and number of tests; amount of blood to be drawn; use of questionnaires; special diet; withholding of standard treatment; follow-up studies; and

randomization, use of placebo, double-blind, or cross-over methods. In the case of patient subjects, state clearly which procedures are experimental and which procedures would be performed for medical reasons if the patient were not a research subject.

3. A description of any reasonably foreseeable risks or discomforts to the subject, their frequency and severity. These may include drug side effects, hazards of procedures, withholding therapy of proven value, financial risk, loss of privacy, or possible detection of genetic predisposition to a disease. Describe what will be done to minimize risks, counteract side effects, and which side effects might be irreversible.
4. A description of any benefits to the subject or to others which may reasonably be expected from participation along with a disclaimer that the investigator cannot guarantee there will be any benefit derived from taking part in the study.
5. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject. It is not necessary to provide a full account of the risks and benefits of standard alternative treatments in the consent document. In some cases, it may be appropriate to state that one reasonable alternative is to choose not to accept any therapy designed to produce cure or remission.
6. A statement describing the extent to which confidentiality of records identifying the subject will be maintained. FDA and sponsor inspection of records in studies involving drugs and devices should be explained. The means of disclosure of information obtained during the study should be described, e.g., publication, entry in medical records, or transmission to another physician and assurance that publication will not lead to personal identification.
7. An explanation that medical treatment is available if a research-related injury occurs. However, if a company or agency sponsoring the research agrees to provide for additional treatment and/or monetary compensation for injuries, this should be included in the consent document.
8. A statement about any costs for which the subject will be responsible and identification of any which are due solely to research. If the research activity will add substantially to the cost of patient care, state this clearly and specifically. It is important to explain to the subject/patient that they might have to pay more money for taking part in the study than they might pay for alternative treatments available and that their physician will discuss with them the costs of the treatment(s) offered through the study as compared to what other treatment might cost. The same applies when there is a disparity of costs between treatment arms (e.g. chemotherapy vs. bone marrow transplant) in the same study. Where applicable the subject should be informed that insurance carriers might not cover costs of research related procedures.

9. A statement of the amount of compensation to be paid to the subject for participation in the research, approximately when they will receive the compensation and the manner in which it will be pro-rated in the event the subject does not complete the study.
10. Identification including the full name(s) and 24-hour phone number(s) of the investigator(s) the subject may contact for answers to questions about the research and the research subject's rights, and whom to contact in the event the subject believes that he or she has sustained a research-related injury. This should include the Institutional Review Board as an agency prepared to identify the patients' rights.
11. A statement that participation is voluntary and that the subject may refuse to participate or may withdraw from the research at any time without penalty or loss of benefits to which the subject is otherwise entitled. When appropriate, subjects should be assured that they will still receive standard treatment if they decide not to participate or to withdraw. They should also be assured that a decision not to participate will not adversely prejudice future interactions with the institution; this is particularly important when a dependent relationship exists between subject and investigator, such as physician-patient, employer-employee, or faculty student. If withdrawal may be dangerous to a subject (for example, abruptly stopping medication that should be tapered.), the danger must be explained and the subject should be told not to withdraw without first discussing it with the investigator.

Additional Elements

The following additional elements of informed consent should be included when appropriate:

1. A statement that the particular treatment or procedures may involve risks to the subject (or to the fetus, if the subject is or could become pregnant) which are currently unforeseeable.
2. Anticipated circumstances under which the subject's taking part may be terminated by the investigator.
3. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue to take part will be provided to the subject.
4. A statement that the investigational drug or device may not be available after the study period.
5. A description of any plan to bank biological specimens or perform genetic analyses, including potential risks.

FORMAT

Language

The consent document should be worded in second or third person active tense (i.e. the participant...) and written in a language that the subject can be expected to understand (simple enough for a sixth grade student), and should not sound nor be coercive.

Two or More Consent Documents

It sometimes is necessary to use two or more consent documents when procedures are to be performed on subgroups of subjects or when reasons for subject selection differ. The most common example of this situation is studies which involve both patients and normal subjects or a treated and a control population. If there is more than one consent document, place a label after the title indicating the subject population to which each is addressed.

Technical Elements

At the top of the first page, the consent document should bear the title of the study, and the name of the institution. Pages should be numbered "1 of 4," "2 of 4," etc. At the end of the consent document there should be statements that the subject will be given a copy of the form to keep. Spaces should be provided for: (a) the signature of the subject who consents to take part; or in the case of a minor, of the parent or guardian who consents on behalf of the subject and a line for the assent of the subject if age 6 or older; (b) the signature of the individual who witnesses the subject's signature; (c) the signature of the investigator or other approved person who enrolls the subject. The witness and the person enrolling the subject cannot be the same person. If someone other than an investigator is to obtain consent, IRB approval is necessary. Additionally, the signature of the witness attests only to the signature of the subject. Unless specifically identified and approved by the IRB, the witness does not act as a consent auditor.

Special Considerations

Banking or Saving Biological Specimens or Creation of Permanent Cell Lines for Future Use.

When the research includes a plan to bank or save biological specimens for future use, the following must be addressed in the protocol and the consent form:

- i. Provide an explanation regarding the purpose of obtaining/saving the sample(s) and indicate not only how they will be used in the immediate research effort, but state that samples will be stored or cell lines will be established from them with the intent to use them in other future research;

- ii. Describe how the subject's confidentiality and privacy will be safeguarded first in terms of how the physical samples and records will be handled in the lab and then how they will be handled when the research is presented or published;
- iii. State who has control over the sample once it is stored in the laboratory. (The sample donor or the investigator) and where there exists a possibility of something being developed of commercial value, whether the sample donor may share in the expected profits;
- iv. If the subject will be able to later withdraw his/her sample from further study, explain what subject should do to make this happen;
- v. give an estimate of the period of time the sample will be kept and used in future research;
- vi. state whether subject will be given any results of the research being done now and or from future research done with their sample(s);
- vii. state whether there is any possibility of third party access to information learned from the samples; and
- viii. clarify whether the subject would be contacted to ask for consent for future research endeavors using his/her specimen or to ask for additional information.

Genetic research

While much genetic research is in very early stages and would not yet have clinical implications, the eventual goal of most genetic research is to discover whether there is a genetic cause for a disease state or a genetic factor that could have treatment implications. DNA can be derived from many easily obtained biological specimens, so the risk associated with genetic research is NOT a physical risk. It is a social and psychological risk. Genetic information pertains to the most personal aspects of individuals' lives and may have implications for family members as well. The research protocol and the consent form must clearly state what type of information will be gained about the disease, its treatment, about the people who have the disease, about the individual tested, about their families and about their children. Subjects need to understand what the implications and what the potential consequences are of obtaining the information sought.

A subject might very well want to be part of the laudable effort to discover the gene that may cause Alzheimer. However, it may never occur to that subject that if it is determined he/she has the Alzheimer's' gene, it might mean that he/she would likely develop the disease. Furthermore, if the results of the genetic research somehow become part of the subject's medical record and the medical record is later reviewed by the health insurance company, and the insurer gives the information to the employer, it could jeopardize the subject's

career. In pedigree studies, non-paternity and non-maternity may also be unexpectedly revealed, changing family relationships forever. Even when DNA is used in research without identifiers, some argue that DNA can never be truly anonymous since each person's DNA is unique, like a fingerprint.

Researchers planning genetic research must address the potential risks to the subjects and their loved ones, state how confidentiality will be safeguarded, indicate how results will be handled, specify the disposition of the biological specimen once the immediate research project is complete and clearly state what information will or will not be shared with the subject.

Deception

The IRB recognizes that in some cases, informing the subject of the hypothesis being tested may result in a biased response. Under these circumstances, the nature of some studies requires that the full purpose not be revealed to a subject until the study has been completed. Such intentional withholding of information may be permitted if the subject is informed that this is the case and agrees. Plans for when and how complete information will be shared with the subject should be disclosed in the consent document.

Pregnancy

If women of childbearing potential are included in a study and there are risks to the woman or fetus, the consent document should describe the test that will be done to determine whether the potential subject is pregnant, the need for contraceptive measures, and known risks of the research to a pregnant woman and fetus. If appropriate, the form should state recommendations about continuation of a pregnancy should the subject become pregnant, and who will bear financial responsibility for the termination of a pregnancy, should the subject and physician determine that this is the alternative of choice.

Screening Studies to Identify Eligible Subjects

If a procedure is to be performed solely for the purpose of identifying a population of research subjects, consent for the screening test and/or process is required. Often, it is appropriate for the screening to be presented in a separate consent document describing the screening procedure and stating that its purpose is to determine eligibility for participation in further studies. A separate consent document for the actual study would then be signed by individuals found to be eligible. In such situations, at the time the subject is enrolled for the

screening procedures, the prospective subjects should be shown the document they will be asked to sign if they prove to meet the criteria for further study.

Distribution and Storage of Signed Consent Documents

A complete copy of the consent document must be given to each subject. A copy with original signatures must be retained in the investigator's file for a minimum of five years after completion of the study.

Guidelines for Subject Consent in Survey Research

Survey research involving the use of self-administered questionnaires and telephone and face-to-face interviews generally places subjects (respondents) at minimal risk. In addition to possible invasion of privacy and disruption of normal routine, the risks can include possible legal risks, possible inconvenience, embarrassment, and other kinds of psychological discomfort. Such risks may become more than minimal when sensitive information (such as sexually transmitted diseases, AIDS, alcohol and drug abuse) is requested.

Self-Administered Questionnaires

A cover letter containing the following information should accompany a self administered questionnaire:

1. An explanation of the purpose of the questionnaire
2. An explanation of how and/or why the subject was asked to participate
3. A statement of the amount of time the questionnaire will require
4. A description of any stresses associated with sensitive information elicited
5. A description of any benefits reasonably to be expected
6. An offer to answer any inquiries concerning the questionnaire
7. An instruction that the subject is free to refuse to fill out the questionnaire
8. An assurance of confidentiality, including how confidentiality will be maintained.

In the instance that there will be no way of tracing respondents, return of the questionnaire to the investigator will be considered to be adequate informed consent provided the cover letter and contents of paragraph (1), above, accompanied the questionnaire.

Telephone and Face-To-Face Interviews

Whenever possible, a letter should precede an interview to inform the subject of the impending interview. The letter should contain the following information:

1. An explanation of the purpose of the interview and the kinds of questions to be asked.
2. An explanation of how and/or why the subject was chosen to participate in the study.
3. A statement of the amount of time the interview will require.
4. A description of any benefits reasonably to be expected
5. An instruction that the subject is free to discontinue the interview at any time without prejudice.
6. An assurance of confidentiality.

At the beginning of the interview, the information contained in the letter should be told to the subject again by the interviewer. Procedures for selection and training of interviewers should be described in the protocol. This should include the number of interviewers to be used, method(s) of recruitment, their familiarity with the community/population to be studied, the language in which the interview is to be conducted, and method of approaching subjects. In the instance of telephone interviews, and assuming that the information letter is part of the process, the oral consent of the interviewee to continue the interview will be considered to be informed consent. In the instance of face to face interviews, the informed consent document should be in writing. Informed consent should be obtained prior to the interview. The signatures of the subject, the interviewer, and the responsible investigator should be contained in the consent document. Like the letter and spoken introduction, the informed consent document should include all the information listed in items 1 through 6 above.

Waiver of Requirement for Signed Consent

The IRB may waive the requirement of **signed** consent in some circumstances, and may require instead that a written statement describing the research be given to the subject. (This does not mean that the consent process is waived).

Such a waiver may be given when one of the following conditions exists:

1. The only record linking the subject and the research would be the consent document and the principal risk would be 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.
2. 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.

Guardian Consent

Unless he/she is also a court appointed guardian or has durable power of attorney to consent for medical treatment, a "next-of-kin" usually cannot give consent for research on an adult subject. Permission for a child to take part in research must be obtained from a parent or legal guardian. Unless waived by the IRB, children who are capable of understanding their involvement in a study should be given the opportunity to assent to the research by signing the assent document in addition to their parents, having been informed of the nature of the project. Generally, age 7 is accepted as the age at which assent is sought. Emancipated minors (those under 21 years of age and married, or those for whom minority status has been court-removed) may consent on their own to take part in research. Although some minors may consent to certain types of medical treatment, there is no legal precedent that they, by themselves, may consent to take part in research.

Child Assent

Adequate provisions must be made for investigators soliciting the assent of children, when the children are capable of providing assent. The ages, maturity, and psychological state of the children involved should be taken into account. Generally, age 6 is accepted as the age children should give assent. If the procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, assent of the children is not a necessary condition for proceeding with the research.

Definitions:

Adult: is a person who has reached legal age. In Puerto Rico this is a person who has reached his/her 21st birthday. For research that includes subjects in other states or countries, other ages may apply. Federal regulations require research activities to comply not only with the Puerto Rico regulations but also with the laws of the state or country where research studies are performed.

Informed Consent is an individual's voluntary agreement, based upon adequate knowledge and understanding of the relevant information, to participate in research either for themselves or for a

minor for whom they have legal responsibility as the parent or legal guardian.

Permission means the agreement of the parent(s) or legally authorized guardian to the participation of a minor in research. This term is often used to emphasize that the parent is not the subject of the research. In this context permission has the same meaning as consent.

Assent means a child's written or verbal affirmative agreement to participate in research. Failure of a child to object to participation cannot be construed as assent.

Minor (Child) is a person, who has not attained the legal age for consent to treatments or procedures involved in research, under the applicable law of the jurisdiction in which the research will be conducted.

Emancipated minor is a person under the legal age who, because of a special situation, has the legal rights of an adult. Situations that qualify a person as an emancipated minor vary by jurisdiction. In Puerto Rico, a married person under 21 years of age is an emancipated minor; pregnancy outside of marriage does not emancipate a minor.

Parent generally means a child's biological or adoptive parent. Foster parents are not authorized to give research consent.

Guardian is an individual, who is legally authorized under applicable state or local law, to oversee the care and management of the child and to consent on behalf of a child to general medical care.

Age guidelines for Assent

The following guidelines, based on the child's age, are usually followed by the IRB in determining assent requirements. Because of the many variables involved in research with children (age, maturity, cognitive ability, degree of study benefit to the child, health of the child, etc.), the guidelines listed below may not be applicable to a specific study and the investigator may propose a different plan. Also, the IRB has the option to require a different approach.

6 Years of Age or Younger, Verbal or Written Assent Is Usually Not Required

Consent is based on the permission of the parent or legal guardian, and no assent is required. A brief verbal explanation of the research procedure should be provided to the child.

Between The Ages of 7 to 14, a Separate Assent Form Is Required

In addition to the parents' consent form, a separate assent form is required for the child. It should be in language appropriate for children 7-14 years of age. The assent form should outline what is involved for the child, and emphasize the voluntary nature of the study. Depending on the research study, it will usually be one to two pages in length. An alternative to written assent is to use verbal assent. Verbal assent is obtained by reading the assent form to the child and obtaining the child's verbal agreement to participate in the study. Verbal assent needs to include the same content as written assent. Further information is available in the section on Verbal Assent.

14 to 21 Years of Age, a Consent or Assent Form May Be Used

Children 14 to 21 years old may give assent by signing the Informed Consent Form that has been signed by the parent(s) or legal guardian. A separate assent form may also be used if the investigator believes it would better inform the child about the nature of the study. This would most likely apply to 14 or 15 year old subjects in very complex studies, or children with mild cognitive impairment

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev.
<p>Administrative Review</p>		

Purpose:

To define the procedure for the administrative assessment of research project applications before IRB review.

Applicability:

IRB Staff

Sources:

OHRP Guidance on Written IRB Procedures

Policy:

The efficiency and effectiveness of the IRB is supported by administrative procedures that allow IRB members to have adequate time for thorough assessment of each proposed research project, and that the documentation they receive is complete and clear in order to facilitate the evaluation of the study design, procedures, and conditions.

Procedure:

Submissions

Upon receipt of an application submitted through the IRB Wise, documents are sorted by category, submission deadline, and assignment to the appropriate IRB panel.

Administrative Assessment

The IRB staff conducts an administrative assessment of all study submissions received from investigators. The purpose of the administrative assessment is to verify the completeness of the application, including submission of all the required documentation and is not an official determination of the IRB.

There are several steps in the process of an application “pre-review” or administrative assessment. First an experienced administrative assistant or “protocol manager“, assesses the submission for completeness, seeking guidance from the IRB Administrator or OPPHI Director as necessary. The submissions will be classified as one of the following:

- Application for New Research Project
- Application for Continuing Review
- Protocol Amendment
- Adverse Event Report
- Final Report / closure letter
- Miscellaneous

Then the documents are sent to another IRB staff member or “pre-screener” for evaluation of the submission content. As part of this administrative assessment, a preliminary determination is made as to the type of review (Full Board, Expedited, or Exempt) required for the particular submission. Assignments to IRB panels, are determined according to the scope of research with consideration given to date received and deadline for submission.

Incomplete Submissions

Incomplete applications are not presented for IRB review until the investigator provides all necessary materials as determined by the IRB staff. The protocol manager through IRBWISE notifies the submitting investigator of any outstanding documentation or additional information requirement before the application is scheduled for review. The protocol manager returns to the investigator those incomplete applications that require substantial revision or additional information. The investigator must complete the request and re-submit the revised application.

Scheduling for Review

Complete applications that appear to meet qualifications for Exempt or Expedited review, are presented to the IRB Chairperson or his/her designee. If a submission meets the Exempt or Expedited review requirements, the review is conducted as described in the SOP for Exempt and Expedite review. All other applications are added to the agenda for the next appropriate meeting for review by the convened IRB.

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev.
Human Subject's Research Determination		

Purpose:

To present the definition of human subject's research applicable to UPR MSC as described under the code of federal regulations.

Sources:

45 CFR 46.102
21CFR 56.102

Applicability:

IRB members, office staff and investigators

Background:

Activities performed by physicians outside of the clinical context may or may not meet the definition for research involving human subjects.

Policy

It is required that all human research studies in which the UPR MSC or affiliated institutions are engaged must be reviewed and approved by the UPR MSC IRB prior to initiation.

Procedure:

The UPR MSC utilizes Code of Federal Regulations' (CFR) Human Subject's Research Definition. Under the CFR (45 CFR 46.102(d)), an activity is considered to be "research" if it involves a "systematic investigation, including research

development, testing and evaluation, designed to develop or contribute to generalizable knowledge.” Activities not systematic, not designed to contribute to general knowledge, or done only for personal or classroom use (i.e. not shared with *anyone* else, including other members of the laboratory or department) do not meet this definition.

Per 45 CFR 46.102(f), research is considered to involve “human subjects” if it entails obtaining information about living individuals, either through intervention or interaction with the individuals or if the research involves the receipt of *individually identifiable* information originally obtained in a context in which the individuals could reasonably expect privacy.

What characterizes an intervention with an individual?

Intervention includes both physical procedures by which data are gathered (e.g., drawing blood) and manipulations of the subject or the subject's environment that are performed for research purposes.

An example of such an intervention would be an educational intervention such as randomly providing pamphlets to some patient-subjects that provide tips for sticking to medication regimens while not providing that information to a set of other patient-subjects with the intent of testing the effectiveness of such a program on increasing compliance with medication schedules.. This type of project involves human subjects because there is an intervention (handing out educational pamphlets) with living individuals.

What characterizes an interaction with an individual?

Interactions include communication or interpersonal contact between investigator and subject.

An example of an interaction with a human subject could be a blood draw or finger stick for research purposes. In this case, there is an interaction with a living individual that is being done outside of the realm of regular patient care.

What is private information?

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 (e.g., medical record information).

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.

What defines a "living" individual?

Since the definition of a human subject is a "living" individual, research which only involves autopsy materials, cadavers or death records is not considered human subjects research and is not reviewed by the IRB.

FDA Definition of Human Subject

FDA regulations (21CFR56.102(e)), define human subject as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient. For research involving medical devices, a human subject is also an individual on whose specimen an investigational device is used.

Some projects, such case reports, research on de-identified human specimens, research on deceased individuals, and quality assurance/quality improvement projects that do not involve drugs or medical devices other than the use of an approved drug or medical device in the course of medical practice or data that will be submitted to or held for inspection by the FDA are not human research as defined above.

It should be noted that other federal, state, or local laws or regulations (i.e. HIPAA), may apply to activities whether or not they meet the definition for research involving human subjects as outlined by 45 CFR 46.

Studies involving deceased individuals

The Health Insurance Portability and Accountability Act (HIPAA) Security and Privacy regulations [45 CFR 160, 164] apply to individuals both living and deceased. Thus, additional protections for subjects may be necessary before beginning a proposed activity (even if the activity does not otherwise qualify as human subjects' research) in order to comply with HIPAA.

In this case, research on decedents may or may not require IRB review. If any protected health information as defined by the HIPAA regulations is collected about deceased individuals, the investigators should submit a complete application on the IRB website. The IRB staff will then determine if further information is required.

Clinical Practice vs. Clinical Investigation

The IRB is aware that research conducted in an academic setting can often result in an overlap between clinical practice designed to take care of a specific patient's medical needs and clinical investigation designed to collect generalizable knowledge to advance standards of care. This distinction can be particularly confusing in clinic-based research where contact with patients and clinical investigators may extend over long periods of time.

The decision as to what constitutes clinical practice in a department is made by the Medical Director. However, in those grey areas where one may be unsure about whether an activity is clinical practice/patient care or research, we encourage faculty to contact the IRB in writing for an opinion. This will avoid any future confusion should the question arise in the course of an application for funding or review of a submitted manuscript for publication of case results

QI/QA Activity

The UPR MSC has adopted the proposed description of quality improvement projects put forth by the National Bioethics Advisory Commission (NBAC) in their December 19, 2000 draft document. Activities that meet the terms explained in the following statements are considered quality improvement/quality assurance activities (QI/QA) at the UPR MSC and do not have to be reviewed by an IRB.

Some data collection and analysis activities in the health services area are not intended to generate scientific knowledge, but rather are used as a management tool to improve the provision of services to a specific health care population (IOM 2000). These activities are not intended to have any application beyond the specific organization in which they are conducted. These activities are generally referred to as program evaluation or quality improvement. But, like public health, because populations are the targets of study and because the methods used in program evaluation or quality improvement are the same as those used in research, it is often difficult to determine whether or not the activity is research that falls under the oversight system.


When the purpose of an activity is to assess the success of an established program in achieving its objectives and the information gained from the evaluation will be used to provide feedback to improve that program, the activity is not human subjects' research. The evaluation is a management tool for monitoring and improving the program. Information learned has immediate benefit for the program and/or clients receiving the program or services. When the quality improvement involving human participants is undertaken to test a new, modified, or previously untested intervention, service, or program to determine whether it is effective and can be used elsewhere, the activity is research. The systematic comparison of standard or non-standard interventions involving human participants also is research.

Public Health Research

The IRB recognizes that surveillance, emergency responses, and program evaluations do not meet the DHHS definition of research. These activities although use systematic methodology, constitute public health activities the

primary intent of which is to prevent disease in a particular population, to improve a public health program, or to provide emergency disaster relief and do not meet the DHHS definition of research. Therefore, these activities do not have to be reviewed by an IRB.

In cases where it is not clear whether an activity falls into clinical practice, QA/QI, or public health research, faculty should request an IRB opinion on whether an activity is research requiring IRB review. The request for opinion should be sent by a letter addressed to an IRB chair. The final determination of the question of whether the activity is or is not a research project is the responsibility of the IRB.

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev. 6/09
<p style="text-align: center;">Procedure for Determining Exemptions</p>		

DHHS regulations describe six categories of research that may qualify for exemption of 45 CFR 46 requirements. Although the regulations do not address a maximum risk level, it is implicit within the concept of exempt research that there must be very little, if any associated risk.

FDA regulation 21 CFR 50.24 defines criteria for exception of informed consent in emergency research. A separate policy below addresses this situation.

Policy:

The IRB retains final judgment for determining if a research activity qualifies for exempt review status. Exemptions may be granted for two groups of activities. The first are those activities that do not constitute research with human subjects as specifically defined by Federal regulations (45 CFR 46.102 (d) (f)). The other group includes those activities designated as exempt by 45 CFR 46.101(b).

To determine if a research activity is exempt from 45 CFR 46 requirements in accordance with the federal policy, the researcher shall complete the electronic application form and submit it to the IRB.

Procedure:

The UPR MSC IRBs are responsible for reviewing the preliminary determinations of exemption by investigators and for making the final determination based on the CFRs. All nonexempt research will be reviewed in accordance with 45 CFR 46.

If an investigator believes that his or her research activities may be exempt from review, the investigator should submit an electronic application through the IRBWISE for the research study indicating the category of exemption requested. The investigator may use a checklist prepared by IRB office and available at <http://irbcm.rcm.upr.edu>, to help assess whether the research meets criteria for requesting exempt review.

The IRB office staff will pre-review the research project application to make a preliminary determination of exemption. Investigators are contacted as appropriate to provide clarification and/or documentation prior to IRB review. Once complete, the application, including all of the supporting documents, is forwarded to the corresponding Chairperson. Only submissions fulfilling all IRB administrative requirements (such as complete proposal, survey instruments and letters of authorization, etc.) will be forwarded for IRB review. The IRB Office will forward submissions to the corresponding IRB Chair at least one week prior to the panel meeting. Urgent Items can be forwarded to any Chair at any time.

The Chair or his or her designee will review the application. If the research is clearly exempt, the investigator will be notified in writing and the decision reported at the next convened meeting of the corresponding IRB panel's and the meeting minutes. If the research is not clearly exempt, and the application contains sufficient information, the request will be forwarded to the IRB Committee for review at its next convened meeting. Research which is not exempt may be suitable for review under expedited review procedures. The investigator will be notified in writing of the final decision.

When research is determined to be exempt, the meeting minutes and the letter to the investigator will include a citation to the applicable regulatory section that was the basis for the exemption.

45 CFR 46 Defined categories for exempt review:

Research in which the only involvement of human participants is in one or more of the following categories may be exempt from IRB review:

a. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

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

c. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:

(i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.


d. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

e. Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine: (i) Public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

f. Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

No research is exempt if any of the targeted populations for this research consists of persons who are:

- legally incompetent;
- significantly mentally ill or impaired; or
- Vulnerable to extraordinary institutional coercion, such as prisoners, residents of 24-hour skilled nursing facilities, or anyone who is involuntarily confined.

	University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office	Effective: 9/1/2008
		Rev. 3/25/09
Procedure for Expedited Review		

Federal Regulations (45 CFR 46.110 and 21 CFR 56.110) define expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research. These regulations define *minimal risk* as the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Policy:

Certain types of research activities, involving no more than minimal risk may be eligible for expedite review 45 CFR 46.110 and 21 CFR 56.110. The IRB chair or a designated member shall determine if a research activity meets the criteria for expedite review.

Procedure:

General Requirements:

All submissions are “pre-screened” by IRB office staff utilizing a checklist of the established categories (45CFR 46 110(a)). If the protocol is considered to meet the criteria for an expedited review, it is sent to the correspondent IRB Chair (next scheduled meeting panel) for verification. Under an expedited review procedure, the review may be carried out by the IRB Chair or Vice-Chair, or by an experienced IRB member, as designated by the Chair.

The person(s) conducting the expedited review may either approve, require modifications (to secure approval) or refer the research to the convened IRB for review in accordance with the non-expedited review procedures, allowing sufficient time for the protocol to be placed on the agenda (24-48 hrs). In

conducting expedited review, the IRB reviewers may exercise all of the authorities of the IRB except that they may not disapprove the research.

The expedite review procedure may not be used where identification of the subject and or their responses would reasonably place them at risk of criminal or civil liability or be damaging the subject's financial standing, employability, insurability, reputation or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

CFR Defined categories for expedited review:

Categories of human subjects research that may qualify for consideration under the expedited review process (as defined in the Federal Regulations) include research activities that (1) present no more than minimal risk to human subjects and (2) involve only procedures listed in one or more of the following categories:

- 1) Research on drugs for which an investigational new drug application is not required or research on medical devices for which a) an investigational device exemption application is not required or b) 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, non-pregnant adults, who weigh at least 110 pounds. For these subjects, amounts drawn may not exceed 550 ml in an 8 weeks period and no more 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/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. Examples: (a) hair and nail clippings in a non-disfiguring manner; (b) deciduous teeth at the 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) un-cannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental

plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

- 4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (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).
- 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.
- 8) Continuing review of research previously approved by the convened IRB as follows:
 - a) where
 - 1) the research is permanently closed to the enrollment of new subjects;
 - b)
 - 2) all subjects have completed all research-related interventions; and
 - 3) 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.


Amendments or modifications or reports on approved research activities

Minor changes to ongoing research activities may be reviewed by an expedited review process. Examples of modifications or reports that may be considered minor under approved research are:

- a. Reports of protocol deviations
- b. Editorial changes to consent forms or recruitment materials that improve readability, or correct typographical errors.
- c. Protocol audit reports, site monitoring reports, protocol sponsor waivers, waivers, sponsor reports and data safety monitoring boards.
- d. Report of protocol deviations
- e. Inclusion or changes in research staff
- f. Sponsor notifications that do not affect directly the Informed Consent Document
- g. Clinical Investigator Brochures and package inserts
- h. Flyers and promotional materials
- i. Other documents related to the study that does not present more than minimal risk to human subjects.

The expedite review procedures **cannot** be used for research involving prisoners.

Information pertaining to submissions reviewed via an expedited review process will be communicated to the full Board on next convened meeting minutes.

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev.
<p>Initial Review- Full IRB Review</p>		

Purpose:

To describe the process of full IRB review at the UPR/MSC.

Introduction:

During the initial review of research, the IRB assesses the proposed protections of the rights and welfare of human subjects participating in research. In order for a project to be approved, it must meet the HHS Criteria for IRB approval of research as defined at 45 CFR 46.111, 21 CFR 56.111 and receive the approval of a majority of the quorum.

Source:

45 CFR 46.111; 45 CFR 46 subparts B,C,D
21 CFR 56.111 21 CFR 50 Sub-part D,

Applicability:

IRB Staff, IRB Members

Policy:

To ensure a thorough review and to provide the greatest protection to our research participants, initial review of research is conducted at a convened meeting where quorum is present, except where expedited review is allowable under the Federal Regulations.

The IRB chair or a designated member shall determine if a research activity meets the criteria for expedite review.

Procedure:

Reviewer system

The UPR MSC IRB utilizes a primary reviewer system. The protocols on agenda for full board evaluations are distributed among the members taking in consideration their expertise, so that each protocol will have a primary and secondary reviewer. The secondary reviewer will substitute the primary reviewer if the later is absent at the meeting, and will otherwise provide an additional level of review and discussion. Treatment protocols will have a physician, nurse or other qualified healthcare professional as the primary reviewer.

Documents distributed to IRB Members before a meeting

Each member will receive an electronic version of the complete agenda and protocols to be reviewed through the IRB Wise system. Each reviewer will be provided an IRB evaluation worksheet to be used as a guide for presenting the protocol during the meeting and given to the office staff after the meeting finalizes.

All the IRB members have special access privileges to the IRB WISE system; therefore they can review all the documents for each study on agenda. At least one week prior to the IRB meeting, each primary reviewer will receive an agenda packet containing paper copies of the application and protocol (refer to policy for IRB submission)

Primary reviewer may request additional information from the Principal Investigator. This can be accomplished directly or through the IRB Office staff. The primary reviewers will present the research project to the convened board at the IRB meeting and address all of the following issues:

- a. Research design and methods
- b. Risk identification and assessment
- c. Benefits identification and assessment
- d. Disclosure of risks and benefits
- e. Plan for data collection storage and analysis
- f. Privacy and confidentiality issues
- g. Equitable selection of subjects

- h. Adequacy of provisions for monitoring and observation of research participants
- i. Adequacy of content, expression and process of informed consent
- j. Requirements for assent

After the primary and secondary reviewers have presented their comments, all Board members discuss the documents received for review and add their comments.

Research or clinical investigations involving pregnant women, human fetuses and/or neonates

For research involving pregnant women, human fetuses and/or neonates, the committee will determine compliance with additional protections of CFR subpart B.

Research or clinical investigations involving children

In the case of research or clinical investigations involving children as subjects, IRB will assess the risk category that applies to the study (as defined on 45 CFR 46 subpart D and if applicable 21 CFR 50 subpart D) and the requirement for parental permission and child assent as follows:

-Studies not involving greater than minimal risk to the children or studies involving greater than minimal risk but presenting the prospect of direct benefit to the individual child subjects involved in the research: Parental permission (one parent maybe sufficient) and child assent according to age guidelines described on “Informed Consent and Child Assent” section of this manual.

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-Studies involving greater than minimal risk and no prospect of direct benefit to the individual child subjects involved in the research, but likely to yield generalizable knowledge about the subject's disorder or condition: Parental permission (both parents unless one is deceased, unknown, incompetent or not reasonably available and child assent according to age guidelines described on “Informed Consent and Child Assent” section of this manual.

Studies that the IRB believes does not meet the conditions described above, but finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children This special cases may not be approved by local IRB and must be referred to DHHS if DHHS funded and/ or to the Commissioner of Food and Drugs, for review.

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Research involving prisoners as subjects:

For research involving **prisoners**, a special checklist will be utilized to assure compliance with CFR sub-part C of CFR.

Determination of Quorum & Voting

Please refer to "IRB Meetings Policies and Procedures" section.

Criteria for IRB approval of Research

The IRB reviews research in accordance with current Department of Health and Human Services (DHHS) and Food and Drug Administration (FDA) regulations. The main purpose of the IRB is to protect the rights and welfare of human subjects who take part in research. More specifically, the IRB assures that:

1. Risks to subjects are minimized.
2. Risks to subjects are reasonable in relation to any benefits that might be expected from taking part in a research study and to the importance of the knowledge that may result.
3. Selection of subjects is fair and equitable.
4. Participation is voluntary and informed consent is obtained from each prospective subject or where appropriate, from the subject's legally authorized representative.
5. The research plan provides for monitoring the data collected to ensure the safety of subjects.
6. There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

Determining frequency of continuing review:

When IRB votes to approve a protocol, they decide the period for which IRB approval is to be granted. This determination is based on their assessment of the degree of risk to participants, as defined in 45CFR 46.103(b) and 109 (e). When the risk is significantly higher in relation to the risk of alternative procedures, IRB will consider requiring more frequent continuing review (periods shorter than a year), or one year with case by case reporting. The approval period begins the day the protocol is approved by convened IRB and must not be longer than a year.


Determining which studies need verification from sources other than the investigators:

Investigators are expected to provide all relevant information regarding the conduct of the research to the IRB. This system is based on trust between the investigators and the IRB. The IRB also relies on Data and Safety Monitoring Boards' (DSMB) reports as an external source of data verification.

In order to assure that the research is conducted in compliance with all regulations for human subject's protection, IRB may require at their discretion verification of information from other sources. Verification of information provided to the IRB may be requested by the convened committee or by the IRB chairpersons during the course of carrying out reviews.

Independent verification may include request and verification of correspondence between sponsor and or FDA and the investigator, including sponsor's audit reports, or direct audits by an IRB-delegated team. This may be considered in the following situations:

- Projects involving unusual levels or types of risk to subjects
- Studies conducted by investigators who had previous non-compliance with regulations
- Unclear or contradictory information noticed during continuing review
- Complaints from subjects or whistleblowers

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev.
<p><i>Institutional Review Board Meetings</i></p>		

Purpose:

The policies in this section provide the framework to ensure that IRB meetings are conducted and documented in a consistent manner in order to meet federal and institutional requirements.

Source:

45 CFR 46.109
21 CFR 56.109

Applicability:

IRB Staff, IRB Members

Background:

The Federal Regulations for Human Research Subject Protection assigns IRB the responsibility to review and the authority to approve, require modification in, table, or disapprove all research activities.

Policy:

The IRB will review proposed research at convened meetings on which a quorum is present, except when an expedited review procedure is applicable. The three IRB panels of the UPR MSC, will alternate in bi-weekly meetings throughout the academic year. Extra-ordinary meetings might be called by Chairperson and the IRB Office Director.

Procedure:

The UPR MSC has three constituted institutional review board panels. Currently IRB meetings are being held every two weeks throughout the academic year. Protocols may be submitted to the IRB at any time, however in order to be considered for IRB review, complete research project applications must be received two weeks prior to the IRB meetings. This ensures that the IRB Committee receives the assigned materials for review on time. In addition to timing, other considerations such as the topic of the research and the length of the agenda are taken to account for assigning a proposal to specific panel's meeting.

A yearly calendar of IRB meetings is posted in the IRB website and distributed to all IRB members by academic year. The Chairpersons of the IRB panels are expected to attend all meetings of the convened Board. The Director of the OPPHI, IRB Administrator or designee and the protocol managers will attend the scheduled meeting.

The agenda for the meeting and all protocol related documents are electronically available to the IRB members. The electronic IRB management system also allows IRB members to conduct electronic reviews. However, for the convenience of IRB members, paper copies of the meeting agenda, along with meeting materials, are also sent to IRB members in advance. Each member of the IRB will also receive a copy of the minutes of the previous meeting. The content of each IRB file is available for all IRB members to review before, during and after the meeting through IRBWISE or at the IRB office.

Determination of Quorum

In order for a research protocol to be approved, it shall receive the approval of the majority of the members present at the meeting.

- A quorum is defined as the majority (50% +1) of the voting members.
- A quorum consists of regular members and/or their alternate members and includes: at least one member whose primary concerns are in scientific areas, and one member whose primary concerns are in nonscientific areas.
- When FDA-regulated research is reviewed there shall be one member who is a physician, nurse or pharmacist.
- An alternate member may attend in the place of an absent regular member in order to meet the quorum requirements outlined above.
- Consultants will not be used to establish a quorum and may not vote with the IRB.

- IRB members who leave the room due to a conflict of interest cannot be counted towards quorum.

Reviewer System

Each protocol on an IRB agenda will be assigned by the IRB Chair to a primary and a secondary reviewer. The primary reviewer will review and present the research proposal at the IRB meeting. Treatment protocols will have a physician, nurse or other qualified healthcare professional as the primary reviewer. The secondary reviewer will substitute for the primary reviewer if the latter is absent at the meeting, but will otherwise provide an additional level of review and discussion. After the primary and secondary reviewers have presented their comments, all Board members discuss the documents received for review and add their comments.

Designated alternates may be used. When alternates are used, the list of Committee members should identify the member(s) for whom each alternate may substitute. To ensure maintaining an appropriate quorum, the alternate's qualifications should be comparable to the member to be replaced. The Committee minutes will document when an alternate replaces a member. When an alternate substitute for a member, the alternate must have received and reviewed the same material that the member received or would have received

Use of Consultants

As the need arises, the IRB may invite individuals with competence in special areas to assist in the review of complex issues that require experience beyond or in addition to what is available on the IRB. These individuals participate in the discussion of protocols but do not vote or count toward the quorum. When consultants are asked to review a protocol, they are asked to disclose to the IRB any conflict of interest related to the protocol. If they do, they will be excused from the review of the protocol and the IRB will identify another consultant.

Voting

Each action to be reviewed and voted upon at a convened IRB meeting requires a quorum, as defined above. To approve an action, a majority (50% +1) of the IRB voting members present must approve. Abstentions count toward the quorum but not toward the required majority. If a quorum should fail during a meeting either due to voting members leaving or because no non-scientist member is present, the IRB will not take any further actions or votes unless the quorum is restored. If the quorum cannot be restored, the meeting adjourns.

After a research project is discussed a motion is made and a vote taken under one of the following categories:

. Approved

1. Approval means that the study may be conducted as presented to the Board.
2. Approval is communicated to the investigator by IRBWISE system followed by an official letter signed by the IRB chair. The letter will specify items and version dates that have been approved.
3. A stamped, approved consent form will be available in the IRBWISE file or included with the letter, if applicable.
4. Requirements for the consenting process will be noted in the letter.
5. Reminders of the Principal Investigators' responsibilities will be defined as footer or an attachment in the approval letter.

. Pending

1. The Board requires minor changes or responses from the investigator for approving the study.
2. The Board may vote to permit a specific reviewer (who has served as the primary reviewer for the study) or the Chairperson to review and accept the requested clarification/revisions.
3. Pending status is communicated by letter to the investigators. Board recommendations are also available at the electronic file to facilitate the process.
4. After the changes are submitted and reviewed, the Board appointed reviewer may recommend approval which will prompt staff to generate an approval letter.

. Deferred

1. The Board has some major concerns which need to be addressed by the Investigator or the Board may require input from a consultant prior to making a decision.
2. Deferral is communicated by letter to the Investigator.
3. The research project must undergo another full board meeting after changes are made.
4. Reasons for deferral must be stated during the research project discussion

. Disapproved

1. The Board denies approval for a specific project after review. A reviewer cannot disapprove a study. This action can only be taken by a convened Board.

2. Disapproval is communicated by letter to the investigator.
3. Reconsideration of disapproval may be requested by the investigator in writing and addressing the letter to the chairperson..
4. Additional information may be made available to the Board before the reconsideration hearing. The investigator may appear before the Board if requested.

. Acknowledged

1. The Board acknowledges through a letter that a requested review has taken place.
2. The letter may request additional information or a response.
3. The Board's acknowledgement does not constitute approval.
4. Future action on the part of the investigator may be outlined in the Board's acknowledgement letter.
5. The Board acknowledges acceptance of the minutes of the previous meetings if there are no perceived discrepancies.
6. The Board acknowledges actions taken by the Expedited Reviewers.

Suspended:

Suspension is when research on an approved protocol is partially or completely stopped by the IRB pending future action. The IRB may find it is in the best interest of the enrolled subjects to allow continued participation in the research interventions or interactions, but enrollment of new subjects cannot occur during IRB suspension. The convened IRB will determine the appropriate actions and if a study is to be terminated. Examples include:

1. occurrence of an unanticipated problem in research involving greater than minimal risk to subjects or others
2. when IRB is investigating a research protocol for issues with serious or continuing non-compliance with federal regulations. Projects that have not recruited subjects and approval have remained suspended for more than six months are to be considered closed.
3. expiration: When continuing review of a research protocol does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically and a project's approval is suspended.
4. by request: Investigators and sponsors may at times need to temporarily suspend a protocol for a variety of other reasons not related to noncompliance or risk to subjects. In these cases, the IRB will suspend the study until the investigator requests in writing that the suspension be lifted. Such suspensions may need to be reported to the Institution as deemed necessary by the Chair or IRB.

Terminated:

The IRB permanently stops research procedures associated with an active approved protocol.

Convened Meeting using Speaker Phone

Only when not otherwise possible to have a quorum, when an IRB member is not physically able to be present during a convened meeting, but is available by telephone, the meeting can be convened using a speakerphone. The member who is not physically present will be connected to the rest of the members via speakerphone. In this manner, all members will be able to discuss the protocol even though one member is not physically present. Members participating by such speakerphone call may vote, provided they have had an opportunity to review all the materials the other members have reviewed

IRB Meeting Minutes

The minutes of each IRB meeting will document the separate deliberations, actions, and votes for each protocol undergoing initial or continuing review by the convened IRB, and the vote on all IRB actions including the number of members voting for, against, and abstaining. The minutes must be sufficient in detail to demonstrate:

Attendance at the meeting, to include:

- If an alternate is present and who they are representing.
- The initial and continued presence of a majority of members (quorum), including at least one non-scientist.
- If a consultant is present

For each protocol discussed, the minutes should describe:


- If a Committee Member is excused from the meeting due to a conflict of interest during the discussion and vote on the study. The name of the committee member is also recorded.
- Actions taken by the IRB.
- Discussion of any controversial issues and their resolutions, including the documentation of the consultant's findings.
- The level of risk (e.g., minimal or greater than minimal).
- Justification for any change in study design or risk level for amendments and continuing reviews.
- The approval period, if less than one year.
- The vote on these actions including the number of voting "for," "against," or "abstaining." (The IRB members at our institution frequently use consensus approach).

- In order to document the continued existence of a quorum, votes should be recorded in the minutes using the following format: Total = xx, For: xx, Against: xx, and Abstained: xx. (Board members who abstain are identified by name in the minutes.)

When protocol revisions are requested or a proposal is disapproved, the basis for the revisions or disapproval is included.

Studies approved under exempt or expedited categories will be included in the corresponding minutes.

When approving research involving children, the meeting minutes must document the risk involved in the research) and that the Committee made the findings in accordance with 45 CFR 46.404, 405, 406 and 407, and 21 CFR 50.51-54. The minutes must also document the assent process, including whether a waiver of assent has been approved, in accordance with 45 CFR 46.408 and 21 CFR 50.55 and 45 CFR 46.116 Subpart A

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev.
<p>Procedure for Continuing Review</p>		

Purpose:

Federal regulations require continuing review of approved research at intervals appropriate to the degree of risk, but not less than once per year.

Applicability:

Investigators, IRB Members, IRB Staff

Sources:

45 CFR 46.109, 113
21 CFR 56.109 (f)

Policy:

The IRB shall conduct periodic continuing review of all approved research projects as deemed necessary, but not less than annually. Continuing review must be substantive and meaningful and must follow the same approval criteria as that for initial review. Investigators are responsible for timely submitting documentation for continuing reviews, or a progress report to close a study file. IRB does not allow for the conduct of research beyond the expiration date of IRB approval.

It is the responsibility of the Principal Investigator to notify the IRB when a study is completed or is being closed. It is important to note that all research activities involving human subjects, including data analysis with individually identifiable or coded private information, must be complete in order to request to terminate

IRB approval for a study. A Final Study Report may be submitted at any time during the review period.

Procedure:

Investigators are required to complete continuing review applications through the IRB management electronic software (IRBWISE). To facilitate timely submission of continuing reviews requests, courtesy electronic reminders that continuing review is required will be sent to investigators prior to the expiration date of the current IRB approval. Investigators must give OPPHI sufficient time to arrange that continuing reviews are seen by the same IRB panel that approved the original proposal and are required to submit renewal requests through the IRBWISE system at least six weeks (1.5 months) before approval expiration date. All sections of the IRBWISE application must be completed. The application must include report and assessment of adverse events (AE) as described in AE reporting policy. In the case of procedural protocol changes a separate amendment application must be submitted. For projects that were planned to be conducted during one year or less, investigators must submit a progress report in a continuing review application to close the file at end of the study. Approved studies that are not submitted for continuing review will be administratively closed after IRB approval period expires.

The IRB must determine that all of the requirements (45 CFR 46.111 and 21 CFR 56.111) are satisfied:

Criteria for IRB approval of Research:

The IRB reviews research in accordance with current Department of Health and Human Services (DHHS) and Food and Drug Administration (FDA) regulations. The main purpose of the IRB is to protect the rights and welfare of human subjects who take part in research. More specifically, the IRB assures that:

1. Risks to subjects are minimized.
2. Risks to subjects are reasonable in relation to any benefits that might be expected from taking part in a research study and to the importance of the knowledge that may result.
3. Selection of subjects is fair and equitable.
4. Participation is voluntary and informed consent is obtained from each prospective subject or where appropriate, from the subject's legally authorized representative.
5. The research plan provides for monitoring the data collected to ensure the safety of subjects.

6. There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

Full Board-Primary reviewer system

In conducting continuing review of research not eligible for expedited review, primary reviewer should at least receive and review a protocol summary and a status report on the progress of the research that includes:

- the number of subjects accrued;
- a summary of any unanticipated problems and available information regarding adverse events (in many cases, such a summary could be a simple brief statement that there have been no unanticipated problems and that adverse events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document, and any investigator brochure);
- a summary of any withdrawal of subjects from the research since the last IRB review;
- a summary of any complaints about the research since the last IRB review;
- a summary of any recent literature that may be relevant to the research and any amendments or modifications to the research since the last IRB review;
- any relevant multi-center trial reports;
- any other relevant information, especially information about risks associated with the research; and
- a copy of the current informed consent document (not stamped) and any newly proposed consent document.

All other protocol related documents are available through the IRBWISE system.

When reviewing the current informed consent document(s), the IRB should ensure the following:

- The currently approved or proposed consent document is still accurate and complete;
- Any significant new findings that may relate to the subject's willingness to continue participation are provided to the subject in accordance with HHS regulations at 45 CFR 46.116(b)(5).

Review of currently approved or newly proposed consent documents must occur during the scheduled continuing review of research by the IRB, but informed consent documents should be reviewed whenever new information

becomes available that would require modification of information in the informed consent document.

Expedited review

When reviewing research under an expedited review procedure, the IRB Chair (or designated IRB member(s)) should receive and review all of the above-referenced documentation. The complete protocol will be available through IRBWISE.

When the study is a clinical trial that is subject to oversight by a monitoring entity (e.g., the research sponsor, a coordinating or statistical center, or a DSMB/DMC), local investigators should submit to IRBs a current report from the monitoring entity.

Closing IRB Approved Research

It is the responsibility of the Principal Investigator to notify the IRB and OPPHI when a study is completed or is being closed. It is important to note that all research activities involving human subjects, including data analysis with individually identifiable or coded private information, must be complete in order to terminate IRB approval for a study. A Final Study Report may be submitted at any time during the review period.

Expiration of IRB approval

. Once a project approval period expires, the Principal Investigator is given an additional 30 days from the expiration date to submit the Continuing Review/Study Closure Report. The IRB chair issues a letter to the investigator indicating that none of the following activities can occur: (1) collection, use, or reporting of any data; (2) performance of any study interventions, unless the IRB finds that it is in the best interests of individual subjects to continue participating in research interventions or interactions; (3) enrollment or screening of any new subjects; and/or (4) receiving any study funding. There is no grace period extending approval for the conduct of research beyond the expiration date. For any project that is allowed to expire and for which a Continuing Review or Study Closure is not received within 30 days of expiration, the project will be moved from “expired” status to “closed” status. To conduct further research on this project, the PI must re-submit the project according to the guidelines for new project submissions.

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev.
<p>Policy for Amendments</p>		

Purpose:

Federal regulations require the UPR MSC IRB to develop processes for ensuring prompt reporting to the IRB of changes in research activities; and for ensuring that changes in approved research, (during the period for which IRB approval has already been given) may not be initiated without prospective IRB review and approval except when necessary to eliminate apparent immediate hazards to the human subjects.

Sources:

45 CFR 46.109
21 CFR 56.109
ICH 3.3.7

Policy:

Changes in approved research, during the period for which approval has already been given, **may not** be initiated without prior IRB review and approval unless when necessary to eliminate **immediate** hazards to the subjects.

Any modifications or changes to the previously approved research protocol must be submitted by the investigator as a protocol amendment. Investigators must promptly report to the IRB any deviation from or changes of the protocol done to eliminate immediate hazards to the study participants. Major protocol violations (as defined below) must be reported to the IRB within 10 days, minor violations are to be reported at continuing review.

IRB determination letters include a statement about the need to have IRB approval for any change in an approved protocol.

Procedure:

Investigators must submit requests for changes in an approved protocol, protocol deviations or protocol exceptions, by completing and submitting a protocol amendment application through IRBWISE. Upon receipt of the protocol amendment application, the IRB Chairperson or designee determines if the revision meets the criteria for expedited review. If the change represents more than a minimal risk to participants, it must be reviewed and approved at a convened meeting of the corresponding IRB panel.

Modifications that do not affect assessment of the risks and benefits of the study or substantially change the specific aims/design of the study are considered minor and qualify for expedited review. Examples of minor modifications include, but are not limited to:

- Addition of research activities that would be considered exempt or expedited if considered independent from the main research protocol;
- Minor increases or decreases in the number of participants;
- Narrowing or broadening the inclusion criteria;
- Changing the formulation (i.e. tablet to capsule or oral liquid) of an administered drug provided that the dose and route of administration remains constant.
- Decreasing the number of biological sample collections, provided that such a change does not affect the collection of information related to safety evaluation.
- Increasing or decreasing the number of study visits, provided the decrease does not affect the collection of information related to safety evaluations;
- Changes in remuneration;
- Changes to improve the clarity of statements or to correct typographical errors, provided that such a change does not alter the content or intent of the statement;
- Addition or subtraction of qualified investigators and/or study sites;
- Minor changes specifically requested by the IRB, or any other campus-based, University committee that has jurisdiction over research.

IRB office staff or Administrator forwards the amendment and related documentation to the IRB Chairperson for expedited review. If the IRB office staff is not certain if an amendment requires full Board review, the Chairperson makes that determination. IRB Chairperson indicates expedited review by signing expedited category list. In the case of expedited review, the IRB staff prints the approval letter and presents it to the Chairperson for signature. The approval is reported in the minutes of the corresponding IRB panel.

In the case of convened Board review, IRB staff for places the amendment on the next appropriate agenda for full Board review. IRB staff prints the appropriate letter based upon the Board action and presents it to the Chairperson for signature.

In the case of emergency protocol deviations, as soon as possible, these must be reported to the IRB including the pertinent details of the situation and the investigators assessment about whether a prospective protocol amendment is in order. The IRBWISE application for amendment form must be used for this type of report.

Applicable Definitions:

PROTOCOL DEVIATION: Any alteration/modification to the IRB-approved protocol. The protocol includes the detailed protocol, protocol summary, consent form, recruitment materials, questionnaires, and any other information relating to the research study.

PROTOCOL EXCEPTION: Any temporary protocol deviation that is approved by the IRB prior to its initiation, e.g., enrollment of a subject who does meet the eligibility criteria.

PROTOCOL VIOLATION: Any protocol deviation that is not approved by the IRB prior to its initiation or implementation.

- **MAJOR VIOLATION:** a violation that may impact subject safety, affect the integrity of study data and/or affect subject's willingness to participate in the study.
- **MINOR VIOLATION:** a violation that does not impact subject safety, compromise the integrity of study data and/or affect subject's willingness to participate in the study.

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 3/19/2007
		Rev.
Report of Adverse Events		

Purpose:

The UPR Medical Sciences Campus requires researchers to comply with all applicable local, state, and federal regulations in the conduct of research studies. As part of this requirement, researchers must submit written reports of events that may represent unanticipated problems or adverse events involving risks to participants and others.

Sources:

21CFR 56.108(b) (1); 21 CFR 312.32(a); 45 CFR 46.103 (a) (b).

Applicability:

Investigators, IRB.

Background:

HHS regulations for the protection of human subjects (45 CFR part 46) contain five specific requirements relevant to the review and reporting of unanticipated problems and adverse events:

- (1) Institutions engaged in human subjects research conducted or supported by HHS must have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and any supporting department or agency head of any unanticipated problem involving risks to subjects or others (45 CFR 46.103(b)(5)).
- (2) For research covered by an assurance approved for federal use by OHRP, HHS regulations at 45 CFR 46.103(a) require that institutions promptly report any unanticipated problems to OHRP.

- (3) In order to approve research conducted or supported by HHS, the IRB must determine, among other things, that:
- (a) 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 subject for diagnostic or treatment purposes (45 CFR 46.111(a)(1)).
 - (b) Risks to subjects are reasonable in relation to anticipated benefits, if any, to the subjects, and the importance of the knowledge that may reasonably be expected to result (45 CFR 46.111(a)(2)).
 - (c) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects (45 CFR 46.111(a)(6)).
- (4) An IRB must conduct continuing review of research conducted or supported by HHS at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research (45 CFR 46.109(e)).
- (5) An IRB must have authority to suspend or terminate approval of research conducted or supported by HHS that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval must include a statement of the reasons for the IRB's action and must be reported promptly to the investigator, appropriate institutional officials, and any supporting department or agency head (45 CFR 46.113).

Federal Regulation 21CFR 56.108(b)(1) requires the IRB to "follow written procedures for ensuring prompt reporting to the IRB...of..."Any unanticipated problems involving risks to human subjects or others..."

Definitions:

Unanticipated problems (UP):

Any incident, experience, or outcome that meets **all** of the following criteria:

- (1) 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;
- (2) related or possibly related to participation in the research. *Possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research; and
- (3) 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.

Adverse event (AE):

Any occurrence that has unfavorable and/or unintended effects on research subjects, regardless of severity or study-relatedness. AEs may manifest as new findings (signs, symptoms, diagnoses, laboratory results) or alterations in pre-existing conditions. AEs must be monitored throughout the entire course of a study, as well as during a reasonable follow-up period after study completion.

- a. **Serious Adverse Events** include death, life threatening adverse experiences, hospitalization or prolongation of hospitalization, disability or incapacitation, overdose, congenital anomalies and any other serious events that may jeopardize the subject or require medical or surgical intervention to prevent one of the outcomes listed in this definition.
- b. **Unexpected Adverse Events** are occurrences that were not anticipated as risks in the IRB-approved protocol and consent form, or occur at a greater frequency or intensity than anticipated.

Policy:

Researchers must submit timely written reports of those events that may represent unanticipated problems and adverse events involving risks to participants and others.

The IRB Chair may at any time suspend research that has been approved by the IRB upon the Chair's receipt of information of any alleged non-compliance with requirements

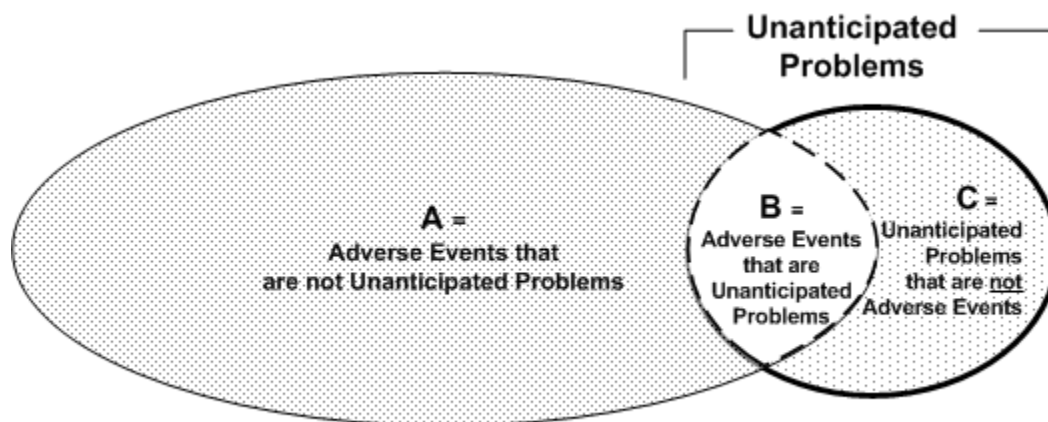
Procedure:

In order to ensure prompt reporting of unanticipated problems or adverse events involving risks to participants or others to the IRB, regulatory agencies, and institutional officials, the IRB requires timely report of the following events:

18.1

- (1) **Unanticipated problems that are serious adverse events** should be reported to the IRB within **1 week** of the investigator becoming aware of the event. In the case of internal (MSC or affiliated institutions) fatal or life-threatening events, these must be reported within **48 hrs**.
- (2) Any other internal **unanticipated problems** should be reported to the IRB **within 2 weeks** of the investigator becoming aware of the problem.
- (3) IRB must report unanticipated problems involving risks to participants to appropriate institutional officials, the supporting agency head (or designee), and OHRP within one month of the IRB's receipt of the report of the problem from the investigator.

The following diagram from OHRP guidance summarizes the general relationship between adverse events and unanticipated problems:



Under 45 CFR part 46: Do not report A; Report B and C.

The diagram illustrates three key points:

- The vast majority of adverse events occurring in human subjects are not unanticipated problems (area A).

- A small proportion of adverse events are unanticipated problems (area B).
- Unanticipated problems include other incidents, experiences, and outcomes that are not adverse events (area C).

18.2 All serious and/or unexpected adverse events that warrant reporting by the above definitions must also be summarized in the Continuing Review. The Continuing Review should contain an assessment of any internal and external AEs reported by the investigator to the FDA and other regulatory agencies since the time of the last review, whether or not the events were considered serious or unexpected at the time of their occurrence.

18.3 It is the responsibility of investigators involved in multicenter protocols to report any serious and/or unexpected AEs (as defined above) in subjects at other sites to the UPR MSC IRB within **10 working** days of their own notification.

Reporting within IRB Wise, using the Adverse Event Report form, is preferred. If access to IRB Wise is not available in the designated time frame, submission of a written report by fax, hand delivery, or express mail to the IRB office is acceptable, as long as the complete report is submitted in IRB Wise as soon as possible.


The IRB Chair or designee will review reports of adverse events. Reports of all internal adverse events that are serious and unanticipated will also be reviewed by the full Board. If an event or problem is determined by the Reviewer and/or Board to raise concerns about risks to subjects or to impact the risk/benefit ratio of the project and is related to the protocol, the IRB may determine that further action is required. Potential actions may include, but are not limited to:

1. A request for clarification of previously submitted information or for additional information from the investigator,
2. Revision(s) to the protocol and/or consent form, (e.g., additional tests or visits to detect similar events in a timely way),
3. A requirement to inform enrolled subjects about changes to potential risks (e.g. re-consent),
4. A change in the continuing review interval,
5. Suspension of new subject enrolment,
6. Additional monitoring by the IRB or designation of a Safety Monitoring Committee,

7. Further inquiry into other protocols utilizing the particular drug/device/procedure in question, and/or
8. Suspension or termination of the study.

Upon making a determination and recommendation for action, the IRB will provide prompt written notification to the Investigator, if applicable, Department Heads, and others. Any findings of any unanticipated problems involving risks to subjects or others (which may include serious, unexpected and related adverse drug/device events) will be reported to applicable Federal Agencies.

The IRB Chair may at any time suspend research that has been approved by the IRB upon the Chair's receipt of information from any source verbally or in writing, of any alleged non-compliance with requirements, determinations, or policies and procedures of the IRB or of any unanticipated problems involving risks to subjects. Before protocols are suspended, any risks to previously enrolled human subjects that will result from suspensions shall be considered. The IRB, IRB Chair, or designee will promptly report any suspension to the Investigator with subsequent written notification generated and reviewed, and approved by the convened IRB. Any suspension or termination of approval will include a statement of the reasons for the IRB's action.

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: June 2009
		Rev.
<p>Investigational New Drug (IND) or Investigational Device Exemption (IDE)</p>		

Purpose:

To define the policy and procedures for the submission of protocols that include the use of investigational new drugs or an investigational device exemption at UPR MSC. To describe the criteria for evaluating the requirement for an IND or IDE.

Applicability:

Staff, IRB members, investigators

Source:

21 CFR 812.2;3

21 CFR 312.2

21 CFR 50;56

Background:

FDA regulations apply to the use of therapeutics, vaccines, and other medical interventions as well as licensed products and devices used for a new purpose. The purpose of the regulation is to assure subject safety & rights and assure that the study is of sufficient quality to permit an evaluation of drug safety and effectiveness. The use of an investigational drug or devices is encouraged by FDA "consistent with the protection of public health and safety and with ethical standards".

Policy:

The use of an experimental drug or device in a protocol is allowable in the Medical Sciences Campus provided it complies with FDA regulations and CFR 21 and GCP.

All research protocols must receive full IRB review and approval prior to implementation.

Definitions:

For the purpose of this policy the following FDA defined terms apply:

IND means an investigational new drug application.

Investigational new drug means a new drug or biological product that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms "investigational drug" and "investigational new drug" are deemed to be synonymous for purposes of this policy

IDE means an investigational device exemption. For most studies involving devices, an investigator or sponsor must obtain an Investigational Device Exemption (IDE) from the FDA..

Investigator means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. "Subinvestigator" includes any other individual member of that team.

Sponsor means a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators.

Sponsor-Investigator means an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor.

Procedure:

Criteria for determination of the requirement of an IND or an IDE:

IRB will determine if an IND or IDE are necessary according to the definitions and regulations in 21CFR 312 and 21 CFR 812. A sponsor shall submit an IND to FDA if the sponsor intends to conduct a clinical investigation with an investigational new drug that is subject to 21CFR312.2 (a). A sponsor shall submit an IDE to FDA if the sponsor intends to conduct clinical investigation with a device as defined in 21CFR 812.

For protocols submitting an IDE, IRB review and considerations will include a risk assessment according to the definitions in 21CFR 812.3. For protocols including an IND the IRB review will be done according to 21CFR 312Subparts B,C,D.

When is an IND needed:

An IND is needed **for all clinical investigations of products that are subject to section 505 of the Federal Food, Drug, and Cosmetic Act** or to the licensing provisions of the Public Health Service Act (58 Stat. 632, as amended (42 U.S.C. 201et seq).

- 1) Studies involving a drug or biologic that is not approved by the FDA
- 2) Studies involving an approved (i.e. commercially available) drug or biologic that is being tested to support a new indication or significant change in the labeling of the drug or biologic.
- 3) Studies involving an approved drug or biologic that is being tested to support a significant change in advertising for the drug or biologic.
- 4) Studies involving an approved drug or biologic that is being tested in a new route of administration, new dosage level, or new patient population that may increase the risk of the drug or biologic.

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

- (i) The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;

(ii) If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;

(iii) The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;

(iv) The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in part 50; and

(v) The investigation is conducted in compliance with the requirements of 312.7.

(2) A clinical investigation involving an in vitro diagnostic biological product is exempt from the requirements of this part if (a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure and (b) it is shipped in compliance with 312.160.

(ii) In accordance regulations, the following products are exempt from the requirements of this part: (a) blood grouping serum; (b) reagent red blood cells; and (c) anti-human globulin.

(3) A drug intended solely for tests in vitro or in laboratory research animals is exempt from the requirements of this part if shipped in accordance with 312.160.

(5) A clinical investigation involving use of a placebo is exempt from the requirements of this part if the investigation does not otherwise require submission of an IND.

(6) A clinical investigation involving an exception from informed consent under 50.24 of this chapter is not exempt from the requirements of this part.

When is an Investigational Device Exemption (IDE) Required

A device is considered investigational if either the device is not approved for marketing in the United States or the device is approved for marketing but is being clinically evaluated for a new indication.

FDA regulations (21 CFR 812.2) state that for studies involving use of an investigational device, the investigator (or sponsor) must obtain either a

"significant risk" Investigational Device Exemption (IDE) from the FDA, or a determination of "non-significant risk" from the institutional review board.

Definition of a Significant Risk Device:

As per 21 CFR 812.3 a Significant Risk Device (SR) as an investigational device that

1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
2. Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
3. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
4. Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

A non-significant risk (NSR) device is one that does not meet the definition of a significant risk device.

To request approval of a protocol that involves an IND or IDE the researcher must include with the IRB application the following:

1. The name and institution of the IND or IDE sponsor,
2. The date it was filed with FDA,
3. IND or IDE number,
4. Written comments from FDA, and written responses to those comments.
5. Risk information from the investigator's brochure, a review of the published literature, or other credible source.
6. Justification for use of the experimental drug or device (e.g., documentation that no available alternative therapy exists)
7. Therapeutic plan (e.g., dose, mode of administration, duration of planned therapy)
8. Provide a high level summary of preclinical data to date including mechanism of action, efficacy and safety.
9. Provide a high level summary of prior human experience with the investigational drug. Include a statement about whether the drug has been withdrawn from investigation or marketing in any country for reason related to safety or efficacy. Cite the reason for the withdrawal.


10. A proposed consent document that meets the criteria described in the informed consent section.
11. Include copies of the applicable forms , exs. FDA 1571,1572,3454,3455
12. In the case of intervention studies done in foreign countries the researcher must include the regulatory oversight of the foreign regulatory body and send written documentation from the regulatory body showing full compliance with local laws.
13. Any other documentation and information requested in CFR21

IRB determinations:

For projects involving drugs and biologics the IRB must assess the requirement of IND based of the criteria defined above.

For projects involving devices the IRB must make two separate decisions, based on different criteria. First: Is the investigation approvable or not? Second: Does the device present significant SR or non-significant risk? If NSR, an IDE can be given by the board. If not, the investigator must be advised to seek a SR IDE from the FDA.

The criteria for deciding if a study involving drugs, biologics or either a significant or non-significant risk device should be approved are the same as those used to evaluate any proposed research project, i.e., the IRB's determination that risks to subjects are minimized, risks to subjects are reasonable in relation to anticipated benefits and knowledge to be gained, subject selection is equitable, informed consent materials and procedures are adequate, and there are acceptable provisions for monitoring the study and protecting patient information.

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev. 6/09
Emergency Use of Experimental Drugs or Devices		

Purpose:

To describe the policies and procedures for the emergency use of experimental drugs or devices at UPR MSC.

Applicability:

Staff, IRB members, investigators

Source:

21 CFR 50.24, 56.109

21 CFR 312.36

Background:

The emergency use of an investigational drug or biologic or unapproved medical device provision in FDA regulations allows for a single use of an investigational drug or biologic or unapproved medical device for a human subject in a life-threatening situation for which no standard acceptable treatment is available and when there is not sufficient time to obtain IRB approval

Planned emergency research conducted in life-threatening situations must be differentiated from the “emergency use” of an investigational drug or biologic or unapproved medical device. For this policy **Planned Emergency Research** defines studies designed for human subjects who are in need of emergency medical intervention but who cannot give informed consent because of their life-threatening medical conditions and who do not have an available legally authorized representative to provide consent.

Policy:

The use of an experimental drug or device for the benefit of a single patient may be approved without delay by the Chair of the IRB provided an emergency situation exists.

Planned Emergency Research is not permitted at UPR Medical Sciences Campus.

Procedure:

The following conditions should exist for a situation to be considered an emergency:

1. The patient is suffering from a life-threatening condition that needs immediate treatment.
 2. No acceptable alternative for treating the patient is available.
 3. Because of the immediacy of the need to use the drug or device, there is not time to use existing procedures to obtain FDA or IRB (full board) approval.
- Requests for emergency use of a drug or device can be made when an IRB-approved protocol exists, but the patient does not meet all eligibility criteria for enrollment (i.e., protocol deviation).

When an approved research protocol does NOT exist, an experimental drug or device can be used on this basis only once and a protocol must be submitted to the IRB within five days. If an investigator anticipates the need to use the drug or device additional times, a protocol must be submitted to the IRB for approval. Data from these activities may only be counted toward research to the extent required by FDA regulations.

Approval to provide emergency medical care for one patient does not constitute IRB approval of the protocol. All research protocols must receive full IRB review and approval prior to implementation.

To request approval for a **one-time** emergency use, send a letter to the IRB, detailing the following:


1. The patient's name and age
2. Physical condition
3. Justification for use of the experimental drug or device (e.g., documentation that no available alternative therapy exists)
4. Therapeutic plan (e.g., dose, mode of administration, duration of planned therapy)
5. IND (investigational new drug)/IDE (investigational device exemption) and the name of the sponsor that is providing the drug or device

6. The name of a physician uninvolved in the patient's care who concurs that the drug or device is needed for a life-threatening situation
7. The name of the hospital in which the patient is to be treated, and
8. A proposed consent document that meets the criteria described in the informed consent section.

In extreme emergencies (minutes or hours), an investigational drug or device may be used without IRB approval provided:

1. The investigator and an uninvolved physician certify in writing in the patient's medical record that the drug or device is needed for a life threatening situation;
2. The patient or the patient's legal representative signs a consent document that meets the criteria, except when the subject is unable to communicate consent and there is no time to obtain consent from the subject's legal representative;
3. If an IND/IDE exists, the sponsor is notified of the emergency use of the drug or device;
4. If an IND/IDE does not exist, the FDA is notified of the emergency use of the drug or device; and
5. A letter describing the situation and a copy of the signed consent document are submitted to the IRB within five days.

Following the emergency use of a drug or device, a written report of the patient's status should be submitted in one week to the IRB.

	University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office	Effective 6/09
		Rev.
Advertisements		

Purpose:

To define the procedure for submission of advertisements for IRB review and approval.

Sources:

- OHRP Guidance on Written IRB Procedures
- 45 CFR 46.111(a)(3)
- 21 CFR 56.111(a)(3)

Applicability:

Investigators, students, IRB members and OPHPR staff

Background:

The FDA and DHHS consider advertising (subject recruitment) to be the first component in the informed consent process. Therefore, the Institutional Review Board (IRB) must review and approve recruitment methods and content of the materials to ensure adequate subject protection. The IRB must review the information contained in all advertisements and the mode of their communication. Advertisements cannot be displayed or put to use until the IRB has approved the final copy of printed ads, the final version of audio/video tape recorded, and final version of electronic media advertisements. As an additional layer of review, the MSC Press Office must approve advertising style and format. Federal regulations require that the institutional human research protection program and investigators protect

potential and current research subjects from coercion or undue influence, and this requirement underpins IRB advertising guidelines. Federal regulations also require investigators to use fair and equitable recruitment practices.

OHRP guidance states that IRBs, in their review of all advertising/recruitment materials, should pay particular attention to risk and potential benefit information to ensure it is presented in a balanced and fair manner. The information presented should not mislead, for example, by promising benefits or implying a benefit beyond that potentially provided by the research. The IRB will assess the types of incentives, if any, that are being offered to prospective subjects. Monetary and nonmonetary incentives (e.g., access to services or programs) can create undue influence on a potential subject's decision about research participation. The IRB will ensure that participation is voluntary, and that incentives for participation are not so great that they compromise a prospective subject's assessment of the risks or affect the voluntariness of his or her choices.

Policies:

1. All advertisement related to research with human subjects require IRB approval before publication in any media and/or form. It must be written in simple language (6th grade reading level). Include the IRB Approval Stamp in the lower right hand corner of the ad. Use of cohesive and/or intimidating language is not permitted in advertisements.

Procedures:

1. Protocols that require the use of advertisement for recruitment of research participants have to include evidence of approval of the advertisement by the MSC Press Office through the IRBWISE system (e-IRB system). Ads are submitted electronically by the investigator through the e-IRB system as part of new protocol submissions and continuing review submissions.
2. An ad must be re-submitted to the IRB for approval when any revisions are made to the IRB approved version of the ad. Investigators must re-submit an ad that has been changed, using the amendment process in the IRBWISE system.
3. For approved studies that did not included the advertisement with the original documentation evaluated and approved by the IRB, the request for advertisement approval has to be submitted as an amendment to the approved protocol.
4. The Advertisement Submission Form found at the IRB website ([Comunicado de Prensa](#)) has to be filled out for each advertisement and must be submitted to the MSC Press Office for their evaluation and

approval prior to consideration by the IRB. All ads must have IRB approval in addition to approval from the MSC Press Office before being exhibited.

5. If the study requires the use of consent and/or assent forms both in Spanish and English, announcements on both languages are required to be approved by both the MSC Press Office and the IRB.
6. For approved studies that did not include the advertisement with the original documentation evaluated and approved by the IRB, the request for advertisement approval has to be submitted as an amendment to the approved protocol.
7. The following may be included in the advertisement:
 - A straightforward description of potential benefits to study participation. Do not overstate.
 - A brief list of procedures involved.
 - The time or other commitment required (number of visits, duration of study, etc.).
 - Any compensation or reimbursement
 - Advertisements may state that subjects will be paid but should not use bold or enlarged print or other means to emphasize payment or the amount to be paid.
 - Do not refer to payment in the header of the ad.
8. The following **MUST** be included in the advertisement:
 - The condition under study and/or the purpose of the research, described clearly and concisely.
 - Clearly state that the project is research and includes the use of an investigational drug or device, if applicable.
 - The key eligibility criteria.
 - The location where the research will be conducted and the contact (name and phone/address) for further information.
9. The following **may NOT** be included in the advertisement:
 - Claims of safety, effectiveness, equivalence or superiority in reference to the drug, device or procedure under investigation.
 - Use of the term “new” in reference to a drug or device without explaining that the test article is investigational.
 - Use of the term “free” in reference to treatment or procedures. Use of bold or enlarged print or other means to emphasize payment or the amount to be paid.
 - Use of exculpatory language.
 - Claims that the subject will receive therapeutic benefit from participation in the study.
 - The use of any inappropriate pictures or images that would be inconsistent with IRB policies on equitable subject recruitment.
 - Offers of compensation from a sponsor that would involve a coupon good for discount on the purchase price of the product once it had been approved for marketing.

- Exhibition of the ad in inappropriate venues.
10. Distribution of ads within the MSC, Puerto Rico Medical Center and University Hospitals
- After IRB approval ads can be posted on the MSCTV network, MSC website and can be placed in designated areas with corresponding management approval. It is the PI's (or his/her designee's) responsibility to coordinate placing posters, flyers and brochures in designated areas with the applicable manager and remove ads at appropriate times.
 - To advertise on the MSCTV network, the PI should contact the CATA Office electronically, by phone or in person (2) weeks prior to air date. CATA Office staff will load and run the ad on the MSCTV network for an agreed upon period of time.
 - For internet posting on the MSC website, the PI must contact the Systems Information Office.

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev.
<p>Conflicts of Interest</p>		

Purpose:

This policy is intended to protect subjects of human research. It is not intended to eliminate all situations of conflict of interest, but rather to enable individuals to recognize situations that may be subject to question and resolve them so as to avoid conflicts of interest. Thus an integral part of the policy is disclosure whereby individuals regularly review their professional activities.

Sources:

DHHS 2004 Final Guidance: Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subjects Protection

Applicability:

Investigators and IRB members

Background:

Public trust in the research enterprise and the legitimacy of its powerful role in society require a constant amenability to public scrutiny. Consequently, it is necessary at all times to assure the continued confidence of the public in the judgment of scholars and clinicians and in the dedication of academic research institutions to the integrity of the research enterprise. The strength of this assurance is based on the assumption that scholars are honest and conduct their research with the highest standards and integrity.

Policy:

- 1) Researchers submitting protocols using human subjects must disclose all interests that may be perceived as a conflict with the best interest of the subject in order for the research to be considered for approval.
- 2) IRB's are also responsible for ensuring that members who review research have no conflicting interest.

Procedure:

Investigators Conflict of Interest

Individuals directly involved in the conduct, design or reporting of research involving human subjects should not have more than a minimal personal financial interest in a company that sponsors the research or owns the technology being studied. A conflict of interest arises when a researcher is or may be in a position to put his or her own interest before the best interests of research subjects. Conflicts involving the IRB itself or conflicts involving the institution must be managed. In order to manage such conflicts, the IRB must be informed of potential conflicts of interest.

Researchers who have completed Financial Disclosure forms required by the FDA to be submitted to a sponsor of the research may submit a copy of that form to the IRB.

Researchers must complete the IRB Wise Conflict of Interest questions in the IRB Wise application. Based on the information submitted by the researcher for review, the IRB may determine that:

- no conflict exists, or
- a conflict exists and must be disclosed to the subjects in the informed consent statement, or
- a conflict exists and the researcher must resolve the conflict before the research can be approved.

Examples of Reportable and Non Reportable Activities

1. Non-Reportable Activities

The following activities and relationships do not need to be reported and do not represent a conflict of interest because they have been generally accepted practices and do not violate fundamental ethical principles.

- Receiving royalties for published scholarly works and other writings.
- Accepting honoraria for commissioned papers and occasional lectures.
- Receiving payment for reasonable travel and lodging expenses related to presentations of scholarly work or to a person's academic endeavor.
- Investing in mutual funds.
- Participating in a University approved corporation.

- Payments for clinical research to an approved practice corporation or to a department fund for salary or other expenses of conducting clinical trials.

2. Reportable Activities

- Conducting research in applied and/or clinical research on a technology developed by the investigator or a member of his/her immediate family (spouse, children, parent, in-laws, and siblings).
- The financial relationship of an investigator or his/her immediate family member with the sponsor of his/her research (acting as scientific advisor or consultant, or receiving honoraria exceeding \$5,000 annually, or acting as director or other executive).
- Conducting applied and/or clinical research on a technology owned by a business in which the investigator or a member of his/her immediate family holds 5% or more of the outstanding stock or stock options.
- Receiving royalties under institutional royalty-sharing policies from marketing the drug, device or procedures that is the subject of the research.
- Receiving payments directly from the sponsor, rather than through the University or an approved UPR MSC entity, for recruiting subjects.


Conflict of Interests among IRB Members

IRB members may not participate in the initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested. IRB Board Members are responsible for making known any potential or perceived conflict of interest concerning protocols reviewed by the IRB. This would include the IRB member's service in any of the following categories with respect to the study in question:

- Principal Investigator,
- Co-Principal Investigator,
- Investigator receiving funding from the study, as listed in the study budget,
- In a supervisory role over the PI of the study, or
- Family member of investigators.

Board members should make known any conflict of interest prior to the beginning of the Board's discussion of the protocol under review. They must leave the meeting room prior to the Board's deliberation and vote.

If the Conflict of Interest status of an individual changes during the course of a study, the individual is required to declare this to their IRB Chairperson and the Director of the HRSPO.

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev.
<p style="text-align: center;">IRB Communication with the Investigators, Institutional Officials and Federal Agencies</p>		

Purpose:

To describe the process of IRB communication with investigators and reporting to the institutional officials and federal agencies

The IRB must timely notify each investigator, in writing, of the outcome of the IRB's review specific to their study. The determination of the IRB, including any conditions of approval, should be clearly stated.

IRB is also responsible to report actions taken about reports of unanticipated problems, protocol suspension or termination, findings of non-compliance with human subject protection regulations, or other actions considered of pertinence to Institutional Officials, OHRP and FDA if applicable.

Applicability:

These policies and procedures apply to all research submitted to the IRB.

Sources:

21 CFR 56.109, 56.113

45 CFR 46.109, 46.113

Guidance on reporting incidents to OHRP/May 27, 2005

Policy:

The Institutional Review Board (IRB) at the University of Puerto Rico Medical Sciences Campus complies with federal regulations and notifies investigators of

all decisions made by the IRB in writing. It is vital that open and frequent communication be maintained between the IRB, the investigator, and the investigator's research team.

IRB actions about reports of unanticipated problems, protocol suspension or termination, findings of non-compliance with regulations or other actions considered of interest to Institutional Officials, are promptly communicated in writing by the IRB office. These actions will also be notified if applicable to the federal agencies (OHRP and FDA).

Procedure:

Communication with investigators

The IRB office utilizes electronic software for the management of the protocols submitted. This software allows the investigators to monitor the status of their protocols, sends reminders for continuing reviews and allows exchange of information between the IRB members, IRB staff and investigators.

IRB decisions are communicated on real time to the investigators through software generated e-mails. These are followed by formal letters signed by the IRB Chairperson. The IRB letters should include the title and protocol number, the IRB decision, and if applicable the rationale for the decision, a list of the issues to be addressed by investigators and the IRB recommendations for addressing these issues.

The IRB notifies the investigator regarding the review decision of all submissions related to new or on-going research projects. These decisions include:

- All recommendations for revisions, additions, or deletions to a research project.
- Notification of an impending continuing review and the outcome of the project once it has been reviewed.
- Actions to withdraw, suspend, or terminate approval for a research project and the reason such action is being taken.
- Status of all adverse events submitted for review.

The OPPHI fosters open communication from the investigator regarding questions, concerns and suggestions as they pertain to the IRB. Questions are answered as promptly as possible and triaged for appropriate responses.

Appeal of IRB Action

An investigator may appeal the revisions required by the IRB in the protocol and/or informed consent form. This appeal must be in writing and submitted to the IRB Chair. Investigators may also appeal an IRB decision to disapprove a study. Any such appeal may be in writing and must be reviewed by the full IRB at a convened meeting. If the appeal is denied and the study disapproved, the Investigator's institution cannot overrule the IRB's decision.

IRB Reports to Institutional authorities, funding agencies and to the Federal Government

Written reports of IRB actions regarding unanticipated problems, protocol suspension or terminations, findings of investigator's non-compliance with human subjects' protection regulations, or other actions considered pertinent to Institutional Officials are prepared by the IRB office staff within a week following the IRB meeting. These reports are forwarded to the investigator's supervisors and the Institutional Official.

The Chancellor of Medical Sciences Campus is the designated Institutional Official as per our Assurance with OHRP. Whenever reports are required to be sent to OHRP and/or FDA they are sent in writing following the guidelines offered by the agency and signed by the Chancellor.

Contact Information for Compliance Oversight:

OHRP

Kristina Borrer
Director
Division of Compliance Oversight
Office for Human Research Protections
101 Wootton Parkway, Suite 200
Rockville, MD 20852

FDA

For Drug Products:

Division of Scientific Investigations (HFD-45)
Office of Compliance
Center for Drug Evaluation and Research
White Oak Campus
10903 New Hampshire Ave.
BLDG 51, Rm. 5341
Silver Spring, Maryland 20993

For Biologic Products:

BioResearch Monitoring Branch (HFM-664)
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research/FDA
1401 Rockville Pike, Room 400S
Rockville, Maryland 20852-1448

For Medical Devices:

Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard – HFZ 403
Rockville, MD 20850

Links to guidelines for reporting incidents:

OHRP

http://www.hhs.gov/ohrp/policy/incidreport_ohrp.html

FDA

<http://www.fda.gov/oc/gcp/irbterm.html>

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev.
<p>Investigators Responsibilities</p>		

Purpose:

To define the responsibilities of a research investigator within the UPR MSC

Sources:

UPR Medical Sciences Campus Federal wide Assurance;
45 CFR 46; Investigational drugs - 21 CFR 312.60; Investigator devices - 21 CFR 812.100; Biologics - 21 CFR 600.10

Applicability

Research Investigators

Policy

The principal investigator is the ultimate protector of the research participant's rights and safety. He or she is responsible to:

- A. Submit a research project for IRB review
- B. Ensure that all human subjects' research receives IRB approval before the research is started
- C. Conduct study in accordance with the approved protocol and consent
- D. Personally conduct or supervise the study
- E. Maintain a protocol file of human research project documents
- F. Comply with Federal and Institutional time periods for record retention
- G. Recruit subjects in an ethical manner
- H. Maintain a protocol file of human research project documents
- I. Ensure that the requirements for obtaining informed consent are met
- J. Respond to subjects who have an adverse event

- K. Keep subjects fully informed of any new information
- L. Provide reports as required by the sponsor and by the IRB
- M. Make records available for inspection
- N. Ensure accountability of investigational drugs, devices, or biologics
- O. Protect the privacy of subjects and maintain the confidentiality of data

Procedure

To serve as the principal investigator on a human subject's research, an individual must be certified in Human Subjects' Protection. He or she must also meet one of the following criteria:

- A credentialed medical staff and/or faculty member of UPR MSC.
- A degree candidate at UPRMSC or a medical resident or fellow. The IRB requires a faculty advisor as co-investigator.
- A non-medical staff person with a UPR MSC appointment such as nurse, pharmacist, etc. The IRB may require a UPRMSC faculty or medical staff to serve as a co-investigator depending on the nature of the study.

If the principal investigator is not a UPRMSC attending physician and the protocol includes treatment at a UPRMSC affiliated facility, a responsible UPRMSC physician- investigator must be identified. The responsible physician investigator must be certified in Human Subjects' Protections.

Investigators may not initiate any research activity involving human subjects without prior IRB review and approval. Therefore, the investigator must have approval prior to publication or presentation of human subjects' research data (e.g., journal article, poster session, public speech or presentation, or project report).

The principal investigator must not institute any changes to the IRB-approved protocol and/or consent form document without first obtaining IRB approval for such changes. The sponsor (if applicable) must also be notified of an investigator's intent to modify the protocol or consent form. In rare instances, an investigator may deviate from the protocol without first notifying the IRB in order to eliminate immediate hazard to a study participant. Any such protocol deviations must be promptly reported to the IRB. Documentation surrounding the event should also be placed in the research record and the medical record if applicable.

The principal investigator may delegate study-related activities, but he or she is ultimately responsible for the conduct of the study. It is the responsibility of each investigator to assure that all procedures in a study are performed with the appropriate level of supervision and only by individuals who are licensed or

otherwise qualified to perform them. Every member of the research team is responsible for protecting participants in research. Co-investigators, study coordinators, nurses, research assistants, and all other research staff have a strict obligation to comply with all IRB determinations and procedures, to adhere rigorously to all protocol requirements, to inform investigators of all serious and unexpected adverse reactions or unanticipated problems involving risk to participants or others, to oversee the adequacy of the informed consent process, and to take whatever measures are necessary to protect the safety, rights and welfare of participants. Regardless of involvement in research, each member of the research community is responsible for notifying the IRB promptly of any serious or continuing noncompliance with applicable regulatory requirements or determinations of the designated IRB of which they become aware, whether or not they are directly involved in the research.

It is the responsibility of the principal investigator to inform all co-investigators about the protocol and consent form. It is also the responsibility of the principal investigator to be aware of any conflicts of interest for any members of the study team. The principal investigator must provide all co-investigators, research coordinators and other research staff with a copy of the current research protocol and consent form and fully inform them of:

- Study procedures (including modifications to the protocol).
- Informed consent requirements and process.
- Potential risks associated with study participation and the steps to be taken to prevent or minimize these potential risks.
- Adverse event reporting requirements.
- Data and record-keeping requirements.
- Current IRB approval status of the study.

Principal investigators must also ensure that if their protocol lists collaborating investigators at another institution that appropriate IRB approval for the study has been obtained at the other institution.

The recruitment of subjects must respect the research subjects' privacy and confidentiality. An investigator should not contact patients who are not in his or her practice unless the patient's physician or caregiver has previously notified the potential research subject (or the parent or legal representative of the potential research subject) and obtained his or her approval for such contact.

It is the principal investigator's responsibility to oversee the informed consent process, making sure that each potential subject fully understands the purpose of the research, the research procedures, the potential risks of study

participation, and his or her rights as a research study volunteer. Informed consent must be obtained prior to the initiation of any study procedure. It is also the principal investigator's responsibility to be sure that anyone obtaining consent from subjects is certified in Human Subjects' Protection and appropriately knowledgeable about the study. The principal investigator is also required to include appropriate additional safeguards in the study to protect research subjects who are likely to be vulnerable to coercion or undue influence. It is the principal investigator's responsibility to assure that potential subjects have the cognitive ability to give consent. To attest to the appropriateness of the subject for the study and the adequacy of the consent process, all consent forms must be signed by the principal investigator within 30 days of the subject signing the consent form.

The principal investigator must maintain a file of human subject's research project documents. The file must include the following items:

- A copy of the human subject's research application submitted to the IRB along with all IRB approvals, amendments, continuing reviews, protocol deviations, and adverse events.
- A copy of the sponsor's protocol (if applicable).
- A copy of the Federal grant application (if applicable).
- A copy of the investigator's brochure for an investigational new drug (if applicable).
- A copy of the investigational device exemption information (if applicable).
- A copy of an investigator-initiated IND or IDE application (if applicable).
- A copy of the consent form with the IRB stamp and expiration date.
- The original of each consent form signed by each participant enrolled in the research. For studies involving inpatients, the investigator is responsible for ensuring that a copy of the consent form is in the patient's medical record.
- A copy of all correspondence with the IRB, sponsor, funding source, FDA, or others.
- A copy of all data derived from the study (case report forms, computer data, adverse event reports, drug/device accountability records etc.)

The principal investigator is required to retain records associated with a human subject's research project. The record-keeping requirements vary depending on whether Federal funding was provided for the project or the protocol was conducted under FDA regulations. The data stored must be kept in a secure, protected manner.

Records for projects that involve FDA regulated articles (drugs, devices, biologics, assays, etc.) must be kept for periods required by FDA regulations based on whether the principal investigator is a sponsor or an investigator.

FDA Regulated Research Investigators

An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects. If the investigation is terminated, suspended, discontinued, or completed, the investigator shall return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR 312.59.

An investigator is required to prepare and to maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual subject administered the investigational drug or employed as a control in the investigation. Case histories include the case report forms and supporting data including: signed and dated consent forms and medical records, progress notes of the physician, the subjects' hospital charts, and the nurses' notes. The case history for each individual must document that informed consent was obtained prior to participation in the study.

Records are required to be maintained for a period of two years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until two years after the investigation is discontinued and FDA is notified.

Investigators must ensure that investigational products are used only for the specific protocol for which they were provided, that each study participant is given specific instructions for their use, and that each subject is following the directions. Investigational products must be adequately and appropriately secured, especially in the case of drugs subject to the Controlled Substances Act. The material should be kept in a locked cabinet or enclosure with limited access.

Confidentiality of Data

It is the responsibility of the investigator to provide a data privacy and confidentiality plan with justification in the protocol on what steps are taken to maintain confidentiality of subject data. The plan must describe how confidential information will be protected from improper use and disclosure. Discussion of maintenance of subject identifiers or a plan to destroy identifiers at the earliest opportunity consistent with the appropriate conduct of the research must be included. Assurances must be provided that confidential (private) information is necessary for the conduct of the research and that this information will not be re-used or disclosed to any other person or entity without written authorization by the subject.

Consent Designees

The principal investigator does not have to obtain consent personally. The study team may include consent designees who are authorized to obtain consent. Consent designees listed on the protocol Checklist (or added to the study by amendment) may obtain consent only after the approval of the IRB for each designee. Each individual who interacts with potential research participants as part of the consent process must have completed Human Subjects' Protections Certification. The principal investigator must ensure that each of these individuals is knowledgeable about the study and capable of answering study-related questions posed by the potential participant.


Participant Complaints/Concerns

The principal investigator is responsible for providing contact information in the consent form to allow participants an opportunity to express complaints or concerns about study procedures or participation. Contact information must be included in the consent form. Complaints received by the IRB will be investigated and reported to convened IRB and institutional official (if, applicable).

The principal investigator is required to retain documentation in the protocol file of any complaints or concerns and their resolution. Serious complaints should be brought to the attention of the IRB when they occur, and all complaints should be reported at the time of continuing review.

Data and Safety Monitoring Plan

For studies that do not have a data safety monitoring board (DSMB), it is the responsibility of the investigator to provide a Data and Safety and Monitoring Plan (DSMP) for the IRB to review as part of the protocol.

	<p style="text-align: center;">University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office</p>	Effective: 9/1/2008
		Rev.
Human Subjects Protection and HIPAA Training Requirements		

Purpose:

To establish the training requirements for research staff under the UPR MSC.

Applicability:

All investigators and research teams

Policy:

All investigators and research team members involved in the conduction of research involving human subjects, shall document they have received training in human research subjects protection regulations and the HIPAA law.

Procedure:

The Principal investigator and all research team members responsible of the design and conduct of human research part of any project, regardless of the funding source, must be trained in Human subjects' protection and HIPAA law prior to project initiation.

The research staff must show evidence of Human Subjects Protection and HIPAA training when applying for an IRB Wise account. The research staff must insert an electronic copy of the training certificate under the investigator's account profile.

UPR MSC is affiliated with the "Collaborative Institutional Training Initiative (CITI program) for the provision of online training for our faculty, students and staff. (citiprogram.org)

IRB also allows the following trainings to satisfy this policy:

- a. Workshop provided by the IRB chairperson.
- b. Workshop provided by a Certified IRB Professional.
- c. Human Subject Protection Training provided by the UPR MSC.
- d. Human Subjects Protection Training provided by recognized institutions (FDA, ARENA, PRIM&R).
- e. Web-based online training
 - Human Subjects:
<http://cme.cancer.gov/clinicaltrials/learning/humanparticipant-protections.asp>
 - HIPAA: <http://irb.ucsd.edu/hipaa.shtml>
- f. IRB 101 Training
- g. Other trainings or tutorials offered by recognized institutions

All members of the research team must have a Human Subjects Protection and HIPAA training for the IRB to grant a final approval of a research project.