WRITTEN POLICIES AND PROCEDURES
FOR THE PROTECTION OF HUMAN SUBJECTS IN RESEARCH

UNIVERSITY
OF MIAMI
Human Subject Research Office
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SECTION 1: PREFACE
These “Written Policies and Procedures for the Protection of Human Subjects in Research” encompass the policies, procedures and operational guidelines for the University of Miami's Institutional Review Boards (IRB) and the Human Subjects Research Office (HSRO) (NOTE – In this document, the term “the IRB” is used to refer to all University IRB’s). In writing and/or revising this document, a goal is to make it an easily comprehensible reference manual for IRB members, for investigators and their staffs, for HSRO staff and for all others who hold an interest in, or who must implement and maintain a commitment to protecting the rights and welfare of human subjects while carrying out responsibilities in human subjects research. For this reason, the restating of federal regulations is minimized. Rather, such regulations that underlie these policies and procedures are usually only referenced within the narrative. Instead, these Policies and Procedures are written and organized to teach and to provide reference to the requirements and best practices in meeting the high ethical standards of the University of Miami and in carrying out federal, state and local regulations.

The importance of written policies and procedures for the proper functioning of Institutional Review Boards and the Human Subjects Research Office cannot be overemphasized. For one thing, written policies and procedures are required by federal regulations (Code of Federal Regulations: Title 45, Part 46.103 (b)(4) and Title 21, Part 56.108(a)). [NOTE – Further such references to federal codes will be made in a shortened manner such as 45 CFR 46.103]. Equally important is that written policies and procedures are essential to:

a. Establish consistency in decisions and decision-making  
b. Promote predictability to investigators and others on the process that the IRB and HSRO will follow  
c. Reduce errors by providing a framework for careful conduct  
d. Give clarity to authorities and responsibilities  
e. Facilitate the training of, and serve as a reference manual for IRB members, investigators, HSRO staff and others  
f. Ensure that human studies research and IRB matters are managed appropriately and equitably

These Policies and Procedures are a “living document” that will be reviewed, revised and supplemented at regular intervals and as needed. This will ensure that they account for advances in methodologies, new concepts of organization, shifts in community ethical standards and changes in regulations. No matter the changes, the goal of these Policies and Procedures shall remain the assurance that human subjects in all research studies of the University of Miami and affiliated institutions receive ethical treatment in concert with the principals of the Belmont Report (i.e. respect for persons, beneficence and justice) federal regulations and the ethical standards of the University and its community of scholars.
Although much effort was expended to make these policies and procedures as complete as possible, it should be expected that matters will be forthcoming for IRB decisions that are not explicitly covered in this document just as this is likely to occur at other institutions. In this circumstance, reference shall be made to existing policies and procedures, and decisions of the IRB and the University shall be guided by federal regulations and the University's ethical standards for the protection of human subjects. A goal shall be to learn from these situations and thereby to improve these policies and procedures to account for such research-related matters in the future. In fact, aren't increasing knowledge and making improvements for societal benefit essential goals of quality research?

Comments and suggestions on the organization and contents of this document and on the effectiveness of the University's human subjects protection program are welcome. These may be addressed to IRB members or to the Human Subjects Research Office (HSRO).

Dushyantha Jayaweera, M.D.

Associate Associate Vice Provost for Human Subjects Research
SECTION 2: BACKGROUND TOPICS
2.1 HISTORY

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: November 30, 2005
Revised: May 10, 2011

Prior to World War II, medical research was performed without appreciable constraints or formal guidance on the protection of the human participants in this research. However, Nazi research atrocities starkly revealed the need to develop basic ethical principles for the protection of human subjects in research and to ensure their oversight. The Tuskegee syphilis study, in which African American men were enrolled without informed consent and were not treated when treatment was available, has further illustrated this need.

Following the Nuremberg Trials, the Declaration of Helsinki was issued. This represented a formal embodiment of ethical principles for the conduct of medical research. It was not until 1966, however, that the U.S. government initiated actions to regulate the performance of human research in this country. On July 1 of that year, William H. Stuart, M.D., Surgeon General, issued Public Health Service Policy and Procedure Order #129, requiring submissions of formal assurances by all institutions conducting human research and thereby establishing the Institutional Review Board (IRB) as a mechanism for ensuring the protection of human research subjects. The National Institutes of Health (NIH) approved the first institutional assurance of the University of Miami on November 1, 1966. In this assurance, the University agreed to establish committees to review all human research studies, and to abide by federal scientific and administrative guidelines and procedures. This Federal Wide Assurance (FWA) has continued to the present day.


The current U.S. system of protection for human research subjects is heavily influenced by the Belmont Report. This Report outlines the basic ethical principles in research involving human subjects. In 1981, with this report as foundational background, the Department of Health and Human Services (DHHS) and the Food and Drug Administration (FDA) revised and made as compatible as possible—under their respective statutory authorities—their existing human subject regulations. With leadership from DHHS, the Federal Policy for the Protection of Human Subjects or the “Common Rule” was published in 1991 and codified in separate regulations by 15 Federal departments and agencies (c.f. Policy 2.3).
The Office for Human Research Protections (OHRP) now oversees any IRBs that review federally funded research involving human subjects while the FDA also oversees IRBs that review studies under its jurisdiction. Knowledge and awareness of human subjects research protections continue to increase; and federal regulations continue to be refined. This is necessary in order to meet the many challenges resulting from the scientific and technological developments that are constantly occurring.
2.2 Ethical Principles

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: November 30, 2005
Revised: May 10, 2011

The Declaration of Helsinki and the Belmont Report provide the ethical foundation for these Written Policies and Procedures. The latter document emphasizes three principles that are central to the ethical treatment of human research subjects and that should guide the conduct of human studies:

a. **Respect for Persons**
   Individuals should be treated as autonomous agents and those persons with diminished autonomy should be entitled to protection. This principle is applied by obtaining informed consent with due consideration of privacy, confidentiality, and additional protections for vulnerable populations.

b. **Beneficence**
   Individuals should be treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. This principle is applied by appropriately weighing risks and benefits.

c. **Justice**
   All individuals should equally share the burdens and benefits of research. This principle applied by the equitable selection of research subjects.

An important aspect of respect for persons is that individuals should be treated as being autonomous. Potential study participants should be given information about a study without undue influence or coercion, so that they can make a reasoned decision on their own. However, there are certain individuals who are particularly subject to influences that may limit their ability to make decisions freely (e.g., children and prisoners). They are considered to be vulnerable and are entitled to additional protections. Respect for persons is particularly relevant to the consent process.

In striving for beneficence, harm should be minimized and benefits maximized. Investigators should attempt to seek alternative ways of investigating hypotheses that would lead to a more favorable risk-benefit ratio.

Justice involves the equitable treatment of human subjects. Thus, care should be taken to avoid performing studies that might cause excessive risks or benefits for one group over another group. In other words, to the extent possible, risks and benefits should be equally distributed. Justice is highly relevant to the selection of research subjects for a study.
In accordance with the above ethical principles, in reviewing research studies, Institutional Review Boards must consider all of the following:

a. The rights and welfare of the individual or group involved
b. The minimization of risks to human subjects by using procedures consistent with sound research design
c. The appropriateness of the procedures and methods employed to the aims, underlying hypotheses and goals of the research
d. The adequacy and appropriateness of the consent form and the process by which consent would be obtained
e. The medical, social or psychological risks to the subject and the reasonableness of these risks in relation to the anticipated medical and/or psychosocial benefits of the investigation, if any, to the subjects and the importance of the knowledge that may reasonably be expected to result
f. The fairness and equitability of the inclusion of individuals according to race, ethnicity, gender, and age

These policies and procedures are based on the shared commitment by the University of Miami and its community of faculty, students, employees and affiliated individuals to the dignity and welfare of individuals who participate in its research. The ethical principles are fundamental to the University's conduct of research.
2.3 FEDERAL REGULATIONS

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: November 30, 2005
Revised: May 10, 2011; June 8, 2011

Until 1991, federal departments and agencies that conduct, support, or regulate research used a variety of policies and procedures to protect human research subjects. To eliminate confusion and promote uniformity, each of these departments and agencies has adopted as regulation a common Federal Policy for the protection of human research subjects. The Federal Policy applies to research involving human subjects that is conducted, supported, or otherwise subject to regulation by any of the following fifteen federal departments and agencies:

1. Department of Agriculture
2. Department of Energy
3. National Aeronautics and Space Administration
4. Department of Commerce
5. Consumer Product Safety Commission
6. International Development Cooperation Agency
7. Agency for International Development
8. Department of Housing and Urban Development
9. Department of Justice
10. Department of Defense
11. Department of Education
12. Department of Veterans Affairs
13. Environmental Protection Agency
14. Department of Health and Human Services
15. National Science Foundation

The FDA has concurred with the Federal Policy, but has additional requirements.

The shared responsibility of all investigators to protect human subjects in biomedical and social/behavioral research from unnecessary risk is codified in Federal rules and regulations governing human research. These are contained in DHHS Code of Federal Regulations 45 CFR 46 (“the Common Rule”) and its subparts B, C and D. [NOTE – Although all federal agencies have adopted the Common Rule, some federal agencies have yet to adopt all subparts]. In addition to the “Common Rule”, human subject research involving drugs, biologics, and devices must comply with FDA regulations found in 21 CFR 50, 54, 56, 312, 600, and 812.
In addition to compliance with federal regulations, the University of Miami and its IRBs are committed to compliance with applicable state and local laws. In taking these and federal regulations into account in its review and oversight of human subject research, the IRB may seek guidance from attorneys in the UM Office of the General Counsel especially when there appears a need for resolution of differences among federal, state and local laws. UM legal counsel may attend IRB meetings and shall have access to study-related documents. Upon request from the IRB, the UM legal counsel shall advise the IRB on any issue/concern that the IRB believes is appropriate to its responsibilities for human subject protection in research including but not limited to: a) whether someone is acting as an agent of the organization; b) whether someone meets the definition of legally authorized representative; c) whether study protocols are compliant with applicable laws/regulations; and d) resolution of conflicts among applicable laws/regulations.
2.4 Federal Wide Assurance (FWA)

**Review Responsibility:** IRB Policy and Procedure Committee  
**Original Approval Date:** November 30, 2005  
**Revised:** May 10, 2011

The University of Miami requires review and approval by an IRB of all research involving human subjects if any UM faculty, staff, or students are engaged as key personnel in that research ("engagement" in research is defined in section 3.7a of this document). Such IRB approval must occur before the involvement of human subjects may begin. The review of research at the University of Miami is conducted in accordance with its Federal Wide Assurance (FWA), which is a binding written agreement with the federal government that is approved by the Department of Health and Human Services (DHHS), Office for Human Research Protections (OHRP) affirming that the University is in compliance with DHHS regulations contained within 45 CFR 46. In studies involving products regulated by the Food and Drug Administration, UM also complies with the requirements set forth in 21 CFR 50, 21 CFR 56, 21 CFR 312, and 21 CFR 812.

Under the FWA, the University commits to DHHS that it will comply with the requirements set forth in 45 CFR 46 as well as 21 CFR 50 and 56 to protect human subjects participating in research. This assurance is required because the University is engaged in human subjects research that is not exempt from the regulations and that is conducted or supported by an HHS agency. Under certain conditions, the University may extend its FWA to cover a collaborating individual investigator.

The FWA states that the University is guided by the ethical principles of the Belmont Report and will comply with federal regulations. The FWA also authorizes registered University of Miami IRB panels to review, approve and disapprove all human subject research projects regardless of funding sources (if any), in order protect the rights and welfare of the subjects through a review process detailed in 45 CFR 46. In addition, the UM IRB has the responsibility and authority to review and take appropriate actions regarding conflict of interest.

The IRB panels at the University of Miami are referred to as the Institutional Review Boards (one or more) for the Protection of Human Subjects in Research involving medical sciences and the Institutional Review Boards (one or more) for the Protection of Human Subjects in Research involving social and behavioral sciences.

The FWA, which is effective for 3 years and which must be renewed at the end of that period of time in order to remain effective, describes the responsibilities of the institution, institutional officer, the Institutional Review Boards, and the investigator.
All investigators at UM are expected to conduct research in accordance with the provisions of the Federalwide Assurance. Primary responsibility for assuring that the rights and welfare of human subjects involved in research are protected rests with the Principal Investigator conducting the research. Faculty members who assign or supervise research conducted by students have an obligation to consider carefully whether those students are qualified to safeguard adequately the rights and welfare of human subjects.
2.5 THE UNIVERSITY OF MIAMI IP³R PROGRAM
(INNOVATIVE PRACTICES FOR THE PROTECTION OF PARTICIPANTS IN RESEARCH)

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: April 4, 2008
Revised: May 10, 2011

These IRB Written Policies and Procedures, together with federal, state and local regulations, address the fundamental ethical principles and goals of human subject protection at the University of Miami and affiliated institutions. In conducting research within these policies, the University and affiliates affirm their commitment to the respect for persons, beneficence and justice in all investigations involving human participants (per the Belmont Report).

These UM IRB Written Policies and Procedures strictly apply federal, state and local regulations (e.g. 45 CFR 46 and 21 CFR 50, 56) to those studies that fall within the purview of those regulations. In considering the application of regulations and policies to other human studies that do not fall within this category, the University recognizes several principles including:

a. participants in research at UM and affiliates shall be afforded protections at least as effective as those defined by federal, state and local regulations and in conformity with the principles of the Belmont Report
b. as for laws, respect for policies requires that policies be respectable (Justice Lewis Brandeis); and common sense often makes for good law and policy (Justice William Douglas)
c. research is ever changing. Policies and processes must account for such changes within an environment that facilitates and encourages the individual nature of each research program. While regulations provide essential guidance for policies and processes of human subject protection in research, the university must consider situations where regulations allow flexibility in policy and procedures which, in turn, may be advantageous to human subjects, investigators and the institution.

The University of Miami applauds the University of Michigan and its trendsetting Demonstration and Initiatives Program. Under this program, policies are being defined that provide ‘equivalent’ protections to human subjects while enhancing efficiency and facilitating human studies. Guided by regulations and the experiences of other institutions including the University of Michigan, and consistent with the principles of the Belmont Report and institutional standards, the University of Miami has implemented its Innovative Practices to Protect Participants in Research Program (the IP³R Program). Goals of this program are to facilitate applicable research, streamline processes, promote efficiency, reduce
bureaucracy and minimize administrative burdens to investigators and reviewers while assuring that institutional human protection resources are allocated to areas where such resources are most needed.

In subsequent sections of these IRB Written Policies and Procedures, individual policies approved by the IRB Policy and Procedures Committee and implemented under the UM IP3R Program will be so identified to distinguish them from policies that are strictly defined by regulations.

**NOTE --** Policies approved under the UM IP3R Program shall not pertain to studies or to training associated with studies that:

a. are under federal jurisdiction pursuant to 45 CFR 46 because support for the study or for training purposes related to the study is derived from federal sources

b. are under FDA jurisdiction pursuant to 21 CFR 50 because the study includes FDA regulated components (drugs, devices or biologics)

c. are under state or local regulations that relate to the ethical standards of research involving human subjects

d. are in receipt of NIH-issued Certificates of Confidentiality

e. are under federally related obligations or contractual restrictions

f. pose more than minimal risk to participants as determined by the IRB

Policies implemented under this IP3R Program are not meant to decrease the protection of human subjects. In fact, the University expects that such policies will result in better protection of research participants by allocating IRB resources with emphasis on the review and oversight of studies pursuant to their risk. Policies approved under the IP3R Program should also encourage compliance as investigators understand that the institution is working to reduce bureaucracy, streamline processes and strengthen the bonds between those who conduct research and those who are responsible for its oversight.

The achievements of the UM IP3R Program must result from a partnership among IRB panels, HSRO staff and investigators. For this reason, all involved in human subject research at UM and affiliated institutions are encouraged to submit suggestions for policies or policy revisions to the HSRO or to Chairs or members of the IRB.
2.6 DOES A PROJECT CONSTITUTE HUMAN SUBJECT RESEARCH

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: July 24, 2006
Revised: May 10, 2011

These written policies and procedures, and the IRB requirement to review and approve/disapprove studies, apply to projects/programs that fit the definitions of 'research' and 'human studies' as derived from federal regulations.

If there is any question as to whether a project or activity constitutes human subject research, the principal investigator/project leader should contact the HSRO for an independent determination which shall be based on the following regulations, policies and the guidance provided by the OHRP in its Chart 1 (reprinted below). Such guidance is based on three questions which are:

a. **Is the activity a systematic investigation designed to develop or contribute to generalizable knowledge?**

Pursuant to 45 CFR 46.102(d), research is defined as a systematic investigation including research development, testing, and evaluation designed to develop or contribute to generalizable knowledge. A key to this definition is that there is a systemic design generally utilizing a scientific approach or protocol for the defined purpose of contributing to generalized knowledge. By this definition, research can encompass studies that are experimental or observational, surveys, tests and recordings whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. Research also includes "clinical investigations" as defined in 21 CFR 50.3(c) which must meet requirements in 21 CFR parts 312, 812, and 813 and require IRB review (21 CFR 56.103).

The definition of research may or may not include public health monitoring activities, internal management studies such as program evaluation, quality assurance or improvement, fiscal or program audits or marketing studies. These activities must be considered on a case-by-case basis to determine if they involve research and require IRB review. Research generally does not include journalism or political polls unless there is clear intent to contribute to generalized knowledge with a scientific protocol. However, the intent to publish may be an indication of intent to contribute to generalizable knowledge.
It is important to distinguish between “research” and the practice of accepted therapy since these may often occur together (such as when research is designed to evaluate the safety and/or efficacy of a therapy). The term “practice” usually refers to interventions designed solely to enhance the well-being of an individual patient or client. Such interventions are carried out with a reasonable expectation of success for purposes of diagnosis, preventive treatment or therapy to a particular individual. In contrast, “research” designates an activity designed to test a hypothesis, permit conclusions to be drawn and thereby to develop or contribute to generalizable knowledge which is usually expressed in theories, principles and statements of relationships. Research is usually described in a formal protocol that contains an objective and a set of procedures designed to reach that objective. If there is any element of research in an activity involving human participants, that activity shall undergo IRB review for the protection of human subjects.

If the activity is not definable as research, then 45 CFR 46 does not apply; but if the activity is definable as research, then a second question should be:

b. **Does the research involve obtaining information about living individuals?**

   Within this definition, “Private Information” includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). “Identifiable Private Information” is that which contains one or more data elements that can be combined with other reasonably available information to identify an individual.

The “obtaining” of identifiable private information or identifiable specimens for research purposes constitutes human subject research. Conversely, research is not considered to involve human subjects when such research involves only coded private information or specimens if both of the following conditions are met:

1. the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; **AND**
2. the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
   a) the key to decipher the code is destroyed before the research begins; OR
   b) the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased; OR
   c) there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; OR
   d) there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased

If an investigator unexpectedly learns the identity of one or more living individuals or now believes that identifying the individuals is important, then the research activity previously considered not to involve human subjects would now involve human subjects and IRB review and informed consent of the subject are required.

If the research does not involve human subjects, then 45 CFR 46 does not apply; but if the research does involve human subjects, then a third question should be:

   c. Does the research involve intervention or interaction with human subjects?
      Pursuant to federal regulation 45 CFR 46.102(f)(1),(2), human subject research is defined as research involving a living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with the individual or from whom an investigator obtains identifiable private information. Within this definition, “intervention” includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subjects’ environment that are performed for research purposes. “Interaction” includes communication or interpersonal contact between investigator and subjects.

Since the University is covered by an approved FWA, all human subject research (as defined above) shall require review and approval by the IRB.
SECTION 3: AUTHORITIES AND RESPONSIBILITIES
3.1 IRB AUTHORITY

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: August 8, 2008
Revised: May 10, 2011

Pursuant to the University of Miami’s commitment to protect human subjects, the University has established one or more panels each called the Institutional Review Board (IRB). Each IRB shall have responsibilities to review assigned human subject research in accordance with federal regulations and each IRB shall have the authority and responsibilities defined within these policies and procedures. In conducting its reviews, each IRB shall be guided by the principles of the Belmont Report, all applicable regulations and the ethical standards of the University.

The UM IRB operates under the regulatory authorities as described within:
1. U.S. Department of Health and Human Services Title 45, Part 46, Subparts A, B, C, and D (for all research, regardless of source of funding)
2. U.S. Food and Drug Administration Chapter I of Title 21 CFR 50 (for FDA regulated research only)
3. U.S. Food and Drug Administration Chapter I of Title 21 CFR 56 (for FDA regulated research only)

The IRB is authorized to review and to approve, defer and/or require modifications to secure approval, table, or disapprove all human subject research overseen and conducted by the University of Miami and covered by the University's Federal-wide Assurance to ensure the rights, welfare and protection of all human subjects. This responsibility extends to all human subject research including pilot studies and feasibility studies, even if such studies include only one subject; and it includes all research involving human subjects performed under the auspices of the University of Miami regardless of whether the studies are extramurally funded, funded by University sources or non-funded. IRB review applies to human subject research conducted by University and Jackson Health System faculty, students, staff, or others, either on the University of Miami/Public Health Trust premises or elsewhere.

The IRB may consider recommendations from other institutional or extramural review committees, but the IRB has the responsibility and sole authority to carry out its review responsibilities in accordance with these policies and procedures.

The IRB shall define whether proposed research is acceptable based on regulations and policies, applicable law, validity of study design as it relates to risks and benefits, sensitivity to community standards and attitudes, as well as standards of professional conduct and practice. No one at the University may approve a study that the IRB has disapproved; and officials of the University may not approve a study if it has not been approved by the IRB [45 CFR 46.112; 21 CFR 56.112]. In order to approve human research studies, the IRB shall review the full proposal, the consent form and all supplemental information such as but not limited to, the sponsor’s protocol (if applicable), investigator's brochure, clinical trial agreement, and recruiting material.
If applicable, each IRB may require studies to be reviewed and approved by ancillary committees such as, but not limited to, the Institutional Biosafety Committee, the Pathology Research Steering Committee, and the Radiation Safety Office. The IRB has additional authorities which include:

a. **Authority to Require Progress Reports and to Oversee the Study**
The UM IRB has the responsibility and the authority to review the progress of human subject research studies, to monitor the activities in approved studies including regularly scheduled continuing review at least annually and to require verification of compliance with approved research protocols and informed consent procedures through means such as audit, observation or third party review. The authority to review the progress of studies includes the authority to require prompt reporting to the IRB of any planned changes in approved projects prior to the implementation of those changes and the authority to require prompt reporting to the IRB of any unanticipated problems (including adverse events) occurring in, or related to, approved protocols.

b. **Authority to Suspend or Terminate Approval of Research**
The UM IRB and/or certain members of the University Administration and/or the IRB chair/designee have the responsibility and the authority to suspend or revoke approval of any study that was originally reviewed and approved for reasons such as unanticipated problems involving risks to human subjects, serious or continuing non-compliance with any federal regulation or serious or continuing non-compliance with the requirements or determinations of the IRB [45 CFR 46.113; 21 CFR 56.113]. Such actions by the IRB shall be determined at a convened meeting of the IRB with a quorum present and shall be incorporated into the minutes of the meeting. The IRB shall consider the rights and welfare of current research subjects when suspending or terminating approval of active studies. (c.f. Section 13).

c. **Authority to Restrict Research**
The IRB has the responsibility and the authority to restrict any study that it has originally reviewed and approved if it determines that such action is warranted. Under this policy, 'restrict' is defined as suspending or terminating a portion of a study found in non-compliance either permanently or until it is brought into compliance. One example of this may be if an aspect of a study fails to comply with federal regulations or IRB requirements or determinations. In this circumstance, the IRB may suspend or terminate approval of the entire study pursuant to the policy on suspending or terminating approval of research (see above) or the IRB may place restrictions on one or more portions of the study. The IRB may also request that a study audit be conducted.

d. **Authority to observe, or have a third party observe, the consent process**
[45 CFR 46.109(e); 21 CFR 56.109(e)]
If an IRB approves a study, that IRB has sole authority for oversight of the study including the consent process. To carry out this responsibility, the IRB may observe or have a third party observe the consent process and/or it may seek information on this process from the principal investigator or others.
e. Authority to observe, or have a third party observe, the conduct of the research  
[45 CFR 46.109(e); 21 CFR 56.109(f)]  
If an IRB approves a study, that IRB has sole authority for oversight of the study including the conduct of the research under the approved protocol.

f. Authority to recommend transfer of IRB responsibility from one IRB to another  
If an IRB approves a study, that IRB has sole authority for oversight of the study. However, there may be occasions when the IRB considers it necessary for another IRB to assume responsibility for oversight of the study. In such instances, the original IRB may recommend, by majority vote at a convened meeting, that the responsibility for the study be transferred to another IRB. This recommendation shall be recorded in the minutes of the convened IRB meeting and forwarded to the Associate Vice Provost for Human Subject Research for review and approval/disapproval.

g. Authority to obtain additional expertise when reviewing a specific study  
If the IRB chair or designee reviewing an exempt or expedited study, or a member of the convened IRB reviewing an initial or continuing study, determines that additional expertise is required for this review, the chair or member has the authority to contact one or more experts within or outside of the University by whatever means he/she believes appropriate or to request that the HSRO arrange for this additional expertise. Review of the specific study requiring this consultative input shall be deferred until the expert advice is received and considered by the IRB.

Guidance/recommendations to the IRB from consultants may be given by personal contact, in writing, by phone, through the internet or other appropriate communication mechanisms. If required and approved by the Associate Vice Provost for Human Subject Research, the HSRO is authorized to arrange for reasonable compensation to consultants.

Verbal guidance/recommendations from consultants provided to the IRB chair or designee conducting expedited reviews shall be summarized by the IRB chair or designee and included within the study file. Written guidance/recommendations from consultants provided to the IRB chair or designee conducting expedited reviews shall be added to the study file. Verbal or written guidance/recommendations from consultants provided to the convened IRB shall be presented at the IRB meeting by the member or other receiving entity and summarized in the meeting minutes. If in writing, such guidance/recommendations from consultants shall be added to the study file.
3.2 HSRO RESPONSIBILITY

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: February 13, 2006
Revised: May 10, 2011

The mission of the UM Human Subject Research Office (HSRO) is to facilitate human subject research among the faculty, staff, and students from all schools and departments within the University of Miami and the Jackson Health System and to support the UM IRB in conducting its reviews and other responsibilities. The HSRO shall be committed to ensuring that University research is conducted according to the University's high ethical standards and in compliance with federal, state and local regulations.

The HSRO is supervised by the Associate Vice Provost for Human Subject Research who is the Institutional Officer of the University. The Associate Vice Provost for Human Subject Research shall ensure that adequate resources (i.e. staff support, equipment, space and other resources) are available and appropriately allocated to and within the HSRO for the HSRO to accomplish its mission. The Associate Vice Provost for Human Subject Research is also responsible for the effective allocation of resources to various activities of the IRB.

The Associate Vice Provost shall ensure that the commitment and performance of HSRO staff and the IRB are evaluated and that standards are met on a continual basis. The Associate Vice Provost shall lead efforts to ensure human subject research regulatory compliance by establishing educational programs, providing relevant resources, ensuring that faculty, staff, students, HSRO staff and IRB members receive the necessary education in the area of human subject protections and in federal, state and local regulations related to human subject protections and by establishing and monitoring quality assurance programs.

The Associate Vice Provost for Human Subject Research shall also ensure the independence of the HSRO and IRB processes such that they are free from coercion and undue influence. IRB members and others with knowledge of undue influence are encouraged to report such to the Associate Vice Provost who shall charge one of the IRBs (without involvement in the allegations) with the responsibility to conduct a thorough investigation and to make recommendations for action, if required, to the Associate Vice Provost for Human Subject Research and to the Executive Vice President and Provost of the University.

The Associate Vice Provost for Human Subject Research has the authority to appoint, reappoint and terminate the appointments of IRB chairs, vice-chairs and IRB members, and to review decisions of an IRB. The Associate Vice Provost for Human Subject Research may administratively disapprove, suspend, or terminate research studies on behalf of the institution. In the case of a decision by the IRB to disapprove, suspend or terminate a project, the decision may not be reversed by the Associate Vice Provost for Human Subject Research or any other officer/agency of UM, state government, or federal government [45 CFR 46.112 and 21 CFR 56.112]. In the case of a decision by the IRB to disapprove,
suspend or terminate a study, the Associate Vice Provost may request that the IRB re-evaluate the study but only because of procedural questions related to the IRB review.

The Associate Vice Provost for Human Subject Research is the signatory Institutional Official responsible for the program of human subject protections at the University and Jackson Health System. The Associate Vice Provost is advised by the Assistant Provost for IRB Affairs who is responsible for coordinating IRB chair practices and interactions among individual IRBs, IRB members and the HSRO. The Assistant Provost for IRB Affairs shall supervise the HSRO when necessary in the absence of the Associate Vice Provost for Human Subject Research and may be designated by the Associate Vice Provost as interim Institutional Officer with signatory authority in the absence of the Associate Vice Provost.

The Associate Vice Provost and the Assistant Provost may attend IRB meetings and participate in deliberations but may not vote and shall not be included in determining or establishing a quorum at the meetings. IRB meeting minutes shall reflect the presence of the Associate Vice Provost and/or the Assistant Provost. In the absence of the Chair or Vice-Chair, the Associate Vice Provost or the Assistant Provost may serve as a non-voting Chair for purposes of administering the IRB meeting.

Specific responsibilities of the HSRO to the IRB and the University include:

1. Assist the IRB in preparing for and monitoring IRB meetings
2. Recommend to the IRB as to whether a study under review constitutes human subject research and if so, the review category for new and continuing studies
3. Forward studies recommended for exempt or expedited reviews to IRB Chairs or IRB-designees for their review
4. Assign studies to the appropriate IRB panel pursuant to the guidance of the IRB chairs and the Assistant Provost for IRB Affairs. Where possible, continuing studies shall be assigned to the original, approving IRB
5. Assign studies to primary and secondary reviewers under guidelines defined by the IRB Chair or IRB-designee and the Assistant Provost for IRB Affairs. Where possible, assignments shall be made to the original, approving IRB primary and secondary reviewers or to similarly qualified members
6. Maintain files on all active human subject research studies (including copies of all correspondence between the IRB and investigators) that take place at the University, JHS and affiliated sites. Following study closure, the HSRO shall maintain for a minimum of three years study files by appropriate storage means that permit subsequent perusal if required. These files may be stored as ‘paper’ files or they may be archived as a microfilm or microfiche, scanned for computer storage or stored within the computer system as submitted
7. Maintain databases for tracking studies
8. Prepare minutes of convened IRB meetings
9. Maintain permanent files of minutes of convened IRB meetings, subcommittee meetings (if applicable) and meetings of the Conflict of Interest Committee
10. Screen research applications for completeness prior to initiating the IRB review process
11. Serve as a resource for investigators on general regulatory information, guidance with forms, and assistance in preparing an application for IRB review
12. Maintain the institution’s FederalWide Assurance and the IRB membership rosters
13. Provide staff support to the IRB for all written correspondence
14. Provide trained staff to serve as administrative-designees of the IRB chair to ensure the correctness of written correspondence and to sign such correspondence as requested by the IRB chair. The individuals selected to serve as administrative-designees shall be approved by the IRB chairs based on skill and training and by the Associate Vice Provost for Human Subject Research.

15. Send notices of study suspension or termination (due to serious or continuing non-compliance) to Principal Investigators and to appropriate University offices.

16. Maintain information on federal regulations relating to human subject research.

17. Facilitate education regarding the IRB process to the University community.

18. Maintain records of IRB membership including training.

19. Maintain the meeting schedule and create agendas for each IRB meeting.

20. Arrange for adequate meeting space for the IRB.

21. Maintain the HSRO web page as a resource for information for the IRB and University.

22. Recommend modifications of these Written Policies and Procedures as necessary to the IRB Policies and Procedures Committee.

23. Ensure that HSRO staff are adequately trained.
3.3 IRB POLICY AND PROCEDURE COMMITTEE

Review Responsibility: Consolidated Medical and Social/Behavioral IRB
Original Approval Date: October 11, 2005
Revised: May 10, 2011

The University of Miami maintains written IRB policies and procedures reflecting current practices of the IRB in conducting reviews and approvals under its Assurance and also reflecting the supporting responsibilities of the HSRO. These policies and procedures were written and implemented with three essential goals:

1. To ensure that the IRB and all institutional employees carry out their responsibilities pursuant to research involving human subjects in compliance with federal regulations and the high ethical standards of the University
2. To provide a clear foundation, and a basis for consistency of, IRB review and actions
3. To provide a structure for training of university faculty and staff, IRB members and HSRO staff

The University has a committee named the IRB Policy and Procedures Committee. The chair of this committee shall be the Associate Vice Provost for Human Subject research who is a voting member of the committee. Voting members are also the IRB chairs and the Assistant Provost for IRB Affairs.

New IRB policies and procedures, or revisions to such policies and procedures, may be recommended by HSRO staff, University faculty and staff, IRB members or the convened IRB, and by the IRB Policy and Procedures Committee. Such recommendations should be addressed to the IRB Policy and Procedures Committee for review. By majority vote, the IRB Policy and Procedure Committee shall approve or disapprove any or all sections of the policies and procedures and/or revisions. The dates of approval and/or revision shall be documented at the top of each section. Changes in IRB policies and procedures are subject to review and approval by the Vice Provost for Research.

It is the responsibility of the IRB Policy and Procedures Committee to ensure that the IRB policies and procedures are reviewed periodically and to ensure that IRB members and HSRO staff are informed of any changes. The Committee shall meet at least annually and shall undertake a review of IRB policies and procedures at least once during a 36 month period.

It is the responsibility of the Associate Vice Provost for Human Subject Research to ensure that these written policies and procedures are provided to all HSRO staff and IRB members and that they are posted on the HSRO website at the University.
3.4 RESPONSIBILITIES OF PRINCIPAL INVESTIGATORS

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: July 8, 2008
Revised: May 10, 2011; June 8, 2011

3.4(a) GENERAL PRINCIPLES

At the University of Miami, human subject research is a privilege, not an entitlement. University policy requires that Principal Investigators and all others involved in University research be aware of the specific responsibilities that they must undertake when conducting research. Principal Investigators and all others engaged in human subject research must comply with these written policies and procedures, all applicable federal state and local laws and regulations, and be guided by the principles of the Belmont report to protect and respect the rights and welfare of individuals who participate in research.

Unless approved by the Associate Vice Provost for Human Subject Research, only UM faculty may serve as Principal Investigators on studies. Jackson Health System employees who obtain approval from the JHS Clinical Research Review Committee (CRRC) may also serve as Principal Investigators on studies. The IRB shall recognize only one Principal Investigator for each project. The Principal Investigator has ultimate responsibility for the administrative, fiscal and scientific conduct of his/her research project and all official IRB correspondence shall be addressed to the Principal Investigator.

Principal Investigators must comply with all requirements for the submission of continuing and final reports and for the proper conduct of the research in compliance with the IRB approval. Failure to comply with IRB requirements for active studies is considered serious non-compliance and may be subject to sanctions including possible termination of approved research. Serious non-compliance shall be reported to the School/College Dean, the Associate Vice Provost for Human Subject Research, Vice Provost for Research and to the Executive Vice President and Provost of the University.

A key responsibility of Principal Investigators is to submit continuing reports in a timely manner to avoid suspension of a study as the result of expiration in IRB approval. As a courtesy, the HSRO shall provide Principal Investigators with prior warning of expiration dates of their active studies. However, it is the responsibility of the Principal Investigator to know expiration dates, to submit continuing review applications with sufficient time for IRB review, and to make necessary changes per regulations if a study is suspended for lapse in approval.
3.4(B) ADDITIONAL RESPONSIBILITIES OF A PRINCIPAL INVESTIGATOR

1. **Education:** Ensure that he/she, co-investigators, sub-investigators, study coordinators, student investigators and all engaged personnel have completed the UM CITI human subject training program, or an equivalent program per approval by the Associate Vice Provost for Human Subject Research, and hold current certification from that program before they participate in the human subject research
   a. Ensure that orientation, education and other in-service sessions take place whenever non-research personnel are involved in areas impacted by the research or whenever such personnel will be contributing data. Examples of such non-research personnel may be hospital nurses or aides, clinical laboratory technicians, cardiology technicians, respiratory therapists etc.

2. **Qualified Personnel:** Ensure that the procedures of the study are conducted by qualified personnel following the approved IRB protocol and maintain a list of appropriately qualified persons to whom significant clinical, trial-related duties have been delegated (“delegation of authority log”)

3. **Amendments:** Ensure that no amendments/changes in the approved IRB application, study protocol or informed consent documents are implemented without prior IRB approval in accordance with UM IRB Policies and Procedures (except in an emergency, if necessary to safeguard the well-being of a human participant. If a change occurs as the result of an emergency situation, the principal investigator must report to the IRB within ten [10] working days of such change).

4. **Exceptions:** Obtain IRB approval prior to the implementation of an exception to a protocol even if that exception pertains only to one or a few participants. If an exception is required in an emergency or life-threatening situation before IRB approval can be obtained, the Principal Investigator must follow the policies defined in these Policies and Procedures for “Emergency Use”. The PI must list all exceptions in the ensuing continuing or final report.

5. **Non-compliance or Protocol Deviation:** Report non-compliance or a protocol deviation to the HSRO within 10 working days of its discovery

6. **Unanticipated Problems and Adverse Events:** Report to the HSRO, and as applicable, to Data Safety and Monitoring Boards, sponsors and appropriate federal agencies all unanticipated problems, including adverse events that occur in the course of research and that increase the level of risk to human subjects or others, within ten (10) working days of the event becoming known to the principal investigator.

7. **Advertisements:** Obtain initial IRB approval for advertisements for the recruitment of subjects and prior IRB approval for any changes in advertisements

8. **Reports, Audits or Reviews:** Ensure that any reports, audits, or reviews of studies performed by outside agencies and sent to the Principal Investigator are submitted to the HSRO within ten (10) working days of receipt by the Principal Investigator. Any reports issued by Data Safety Monitoring Boards (or similar entities), whether inside or outside the University, must also be submitted to the IRB within ten (10) working days of receipt by the Principal Investigator.
9. **Research Files:** Maintain research files for a minimum of three years (or longer according to the sponsor’s requirements if applicable) from the date of study completion including:
   a. All correspondence with the IRB and the sponsor (if applicable)
   b. Documentation of subject eligibility
   c. Copies of signed consent forms obtained from all subjects participating in and/or who have participated in the protocol regardless of whether the subject completed the study.
   d. Any data derived from the study
   e. In addition, principal investigators must maintain any authorization documents to use or disclose private health information (PHI) for a minimum of six years from the date authorization is obtained

10. **Informed Consent:** Ensure that the legally effective informed consent is obtained from human participants or their legally responsible representative. If the IRB has required written consent, use only the IRB-approved, date-stamped/watermarked informed consent documents
   a. Ensure that each subject or their legally responsible representative receives a copy of the signed consent form and that a copy of the signed consent form is inserted into the research file and/or if the subject is a patient, a copy of this form should be placed in his/her medical record.

11. **Compliance:** Ensure that all members of the research team always comply with the findings, determinations and requirements of the IRB

12. **Recruitment Locations:** Fully inform the IRB of all locations in which human participants will be recruited for the study and ensure that current IRB approvals/letters of cooperation are obtained and maintained when applicable

13. **Suspension/Termination:** Ensure prompt and complete compliance with any IRB or administrative decision to suspend or withdraw approval for the study

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**3.4(c) INVESTIGATOR’S RESPONSIBILITY SHEET**

To assist Principal Investigators and remind them of their responsibilities, the HSRO will include a brief review of the principal investigator's responsibilities within the "Principal Investigator's Assurance Statement". This Assurance Statement constitutes the concluding page of the computer-based forms that must be signed and submitted by the Principal Investigator to the IRB for new studies, continuing reports, amendments and reportable events. By signing this Assurance Statement, the Principal Investigator shall affirm that he/she has ultimate responsibility for the conduct of the research described therein, the ethical performance of the project, the protection of the rights and welfare of human participants, strict adherence to the study protocol and for any stipulations imposed by the UM IRB. The PI's signature shall also affirm that the PI is knowledgeable of and agrees to comply with all regulations and institutional policies regarding the protection of human participants in research.
3.5 RESPONSIBILITIES OF UM DEANS/DEPARTMENT CHAIRS

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: December 19, 2006
Revised: May 10, 2011; June 8, 2011

It is the responsibility of the academic department chairperson (or Dean in a non-departmentalized School of the University) and other University officials (such as Center Directors for studies being conducted within the facilities or with support from that Center) to assist in ensuring that IRB determinations are followed. Submission of a study or study amendments for IRB approval shall require that these persons or their designees grant permission for that submission via ePROST (electronic signature) noting that he/she certifies that the research study referenced in the study application or amendment is well designed and scientifically sound. This permission shall also be confirmation that appropriate financial and other necessary resources are available, that the credentials of all persons engaged in the research are appropriate and that investigators have sufficient time to carry out their study commitments and oversee conduct of the research.

It is also the responsibility of the academic department chairperson (or Dean in a non-departmentalized School of the University) to inform the IRB of situations that may preclude a Principal Investigator from continuing in his/her role as Principal Investigator and to recommend to the IRB any changes of Principal Investigator for ongoing studies in which the original Principal Investigator is either unwilling or unable to continue in this position.
3.6 RESPONSIBILITIES OF STUDENTS AND FACULTY ADVISORS

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: February 13, 2006
Revised: May 10, 2011

Students/trainees/fellows may serve as Principal Investigators in human subject research (e.g. dissertation, thesis or other research studies) if prior approval is given by the Associate Vice Provost for Human Subject Research. Such approval requires that the study be submitted under faculty supervision. The supervising faculty member must indicate his/her acceptance of the responsibilities as faculty advisor and assure that he/she will oversee the Principal Investigator in complying with the responsibilities of a Principal Investigator.

Faculty advisors shall affirm that the student/trainee/fellow is knowledgeable about the regulations and policies governing research with human participants and has sufficient training and experience to conduct the particular study in accordance with the approved protocol. Also, the Faculty Advisor shall meet with the Principal Investigator (student/trainee/fellow) on a regular basis to monitor study progress and to ensure compliance with UM policies and federal regulations.

If a faculty advisor becomes unavailable to supervise the approved study, such as when on sabbatical leave or vacation, the faculty advisor must arrange for an alternate faculty advisor to assume direct responsibility and notify the IRB via an amendment in advance of such arrangements.
3.7 CITI CERTIFICATION

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: February 7, 2006
Revised: May 10, 2011

3.7(A) GENERAL PRINCIPLES
Federal regulations and guidelines require documented evidence that IRB members, principal investigators, co-investigators, collaborators, study coordinators and/or other individuals involved in human subject research are qualified and have the expertise needed to protect human subjects. To meet this requirement and University ethical standards, University of Miami policy requires that all IRB members and those individuals considered to be engaged study personnel receive and maintain "CITI certification" (or its equivalent) in human subject protection prior to their involvement in human subject research. This applies to existing and new personnel.

Pursuant to the above requirement, individuals are considered to be "engaged in human subject research" if they make a direct and significant contribution to a particular study and/or to the conduct of protocol requirements or who contribute in a substantive way to the scientific development of a project. This definition includes (but is not limited to) individuals who have direct contact with subjects, identifiable subject data, identifiable subject records, protected health information or identifiable biological samples collected and/or tested for research purposes. Engaged personnel also includes clinical professionals who administer any study-related intervention being tested or evaluated under a research protocol. Engaged personnel are also those listed as such on a DHHS-supported grant that is sponsoring the study. Students are considered engaged personnel if they meet any of the criteria described in this paragraph. The definition of engaged personnel is not dependent upon whether or not the personnel receive compensation from the grant supporting the project.

The definition of engaged personnel does not include:
1. individuals who have direct contact with subjects, subject data, subject records, protected health information or biological samples collected and/or tested for research purposes on a commercial basis pursuant to a contractual fee-for-service arrangement
2. individuals who only contribute to the scientific development of a project unless: (1) they have direct contact with subjects or identifiable data; or (2) they have potential financial interest in the outcome of the research.
3. clinical professionals who are simply performing a service typically required of their position (i.e. blood draw, infusion, chemo) and who are not contributing to the research in a substantive way such that:
   (a) the services performed do not merit professional recognition or publication privileges;
(b) the services performed are typically performed by those clinical professionals for non-
research purposes; and
(c) the clinical professionals do not administer any study intervention being tested or
evaluated under a research protocol.

The following are some examples, assuming the services described would not merit professional
recognition or publication privileges:

- an appropriately qualified laboratory whose employees perform routine serum chemistry
  analyses of blood samples for investigators as a commercial service.
- a transcription company whose employees transcribe research study interviews as a
  commercial service.
- a hospital whose employees obtain blood through a blood draw or collect urine and provide
  such specimens to investigators as a service.
- a radiology clinic whose employees perform chest x-rays and send the results to investigators
  as a service.

The University of Miami is a leader in developing educational programs to train its faculty, staff and
others in the regulations and responsibilities of human subject research and to raise the level of
awareness to human subject protection issues. The web based Collaborative IRB Training Initiative
(CITI) Program in The Protection of Human Research Subjects is hosted and administered by the
Office of Research Education at the University of Miami and provided to over 550 institutions around
the world. The course is available 24/7/365, it is accessible from any office or home computer and it
provides a “user friendly” presentation model and assessment tools.

Completion of the CITI "Core" Course (at least one from Groups 1-4) is required to become certified to
conduct human subject research at the University of Miami. Re-certification is required at two-year
intervals and is accomplished by completing the CITI Continuing Education course.

It is the responsibility of the Principal Investigator to ensure that all engaged personnel are currently
CITI-certified before they can participate in human subject research. UM key personnel may take the
Collaborative IRB Training Initiative (CITI) online (accessible from the HSRO website) for certification or
receive certification from other equivalent programs approved by the Associate Vice Provost for Human
Subject Research. Re-certification of engaged personnel must be conducted as required. A CITI
certificate issued by another institution may be honored at UM if all UM-required modules were
completed with the UM-required total passing score.

For studies initiated by students pursuant to dissertation requirements, the faculty member who serves
as the principal investigator (or who is the faculty advisor if the student serves as principal investigator)
and the student-investigator must both hold current CITI-certification. Dissertation committee members
who meet the UM definition of engaged personnel must also hold this certification. Dissertation
committee members who are involved only as mentors or advisors without direct subject contacts or
other responsibilities of engaged personnel are not required to hold CITI certification.
3.7(B) OPERATIONAL POLICY

Training for certification is provided through the University's Collaborative IRB Training Initiative Program (CITI Program) which was developed by UM and national experts in bioethics and the IRB process.

It is essential that position descriptions submitted to the Human Resources Office for individuals involved in human subject research include the requirement for CITI certification within 30 days of hire. This requirement should also be included in offer letters to candidates. Open positions currently in the Human Resources Office that include human subject research activities require an updated job description to include the requirement for CITI certification. If required certification is not obtained within the first 30 days of hire, the staff member must not be permitted to participate in human subject research and shall be subject to disciplinary action up to and including termination.

Please know that the CITI Program offers excellent courses for new certifications; all personnel involved in human subject research must complete at least one of the following courses to become "CITI-certified":

1. **CITI Biomedical Course**: Required for all personnel involved primarily in biomedical research; and for all personnel performing both biomedical and social/behavioral research

2. **CITI Social/Behavioral Course**: Required for all personnel involved primarily in social and behavioral research. The IRB reserves the right to make this course a requirement for research personnel involved in both biomedical and social/behavioral research

The program courses are grouped so that investigators and others can choose one of the relevant training courses based on the following criteria:

**Group 1** is for investigators and staff who:
- Have **direct contact** with subjects or with subject records
- Are involved in drug or device studies
- Work **ONLY** at/with the U of Miami/Jackson Hospital

**Group 1 with VA affiliation** is for investigators and staff who:
- Have **direct contact** with subjects or subject records
- Are involved in drug or device studies
- Work at/with **BOTH** the U of Miami/Jackson Hospital AND at the Miami VA Hospital

**Group 2** is for investigators and staff who:
- Have **direct contact** with subjects or subject records
- Are **NOT** involved in drug or device studies
- Work **ONLY** at/with the U of Miami/Jackson Hospital
**Group 2 with VA affiliation** is for investigators and staff who:

- Have **direct contact** with subjects or subject records
- Are **NOT** involved in drug or device studies
- Work at/with **BOTH** the U of Miami/ Jackson Hospital and at the Miami VA Hospital

**Group 3** is for investigators and staff who:

- Have **NO clinical contact** with subjects
- Conduct records based research or laboratory research with biological samples
- Work **ONLY** at/with the U of Miami/Jackson Hospital

**Group 3 with VA affiliation** is for investigators and staff who:

- Have **NO clinical contact** with subjects
- Conduct records based research or laboratory research with biological samples
- Work at/with **BOTH** U of Miami / Jackson Hospital AND at the Miami VA Hospital

**Group 4** is for investigators and staff who:

- Conduct **Social/Behavioral Research** only
- Have **direct contact** with subjects or subject records
- Work **ONLY** at/with the U of Miami

**Group 4 with VA affiliation** is for investigators and staff who:

- Conduct **Social/Behavioral Research** only
- Have **direct contact** with subjects or subject records
- Work at/with **BOTH** U of Miami AND at the Miami VA Hospital

**Group 5** is for IRB Chairs, IRB members and alternate members, HSRO administrators and HSRO staff only

Upon successful completion of the appropriate CITI course including the corresponding groups as listed above, research personnel will be "CITI-certified" for a period of two years. Re-certification is required within two years of the initial CITI-certification.

IRB members who do not engage in human subject research and HSRO staff who complete Group 5 will be “CITI-certified” for a period of three years. Re-certification is required within three years of the initial and/or last CITI-certification. HSRO staff and others who are Certified IRB Professionals (CIP) are exempt from the CITI certification requirement as CIP re-certification is required every three years.
To improve efficiencies and streamline processes, efforts are underway to integrate CITI certification records into the eProst system which is central to the management of human subject-IRB information and processes.

For questions or concerns related to this issue, please contact the Human Subject research Office at 305-243-3195 or email the HSRO Help desk at eprost@med.miami.edu.
SECTION 4: CONFLICT OF INTEREST
4.1 **GENERAL PRINCIPLES**

**Review Responsibility:** IRB Policy and Procedure Committee

**Current Approval Date:** October 27, 2006

Objectivity is essential to the conduct of scientific research and the basis for public confidence in the integrity of IRB oversight and the research enterprise. Research must not be led by interests that might undermine scientific integrity and ethical values. It is recognized that success in research brings rewards including publications, grants, career advancement and the satisfaction of accomplishment. Research may also bring financial gain through industry sponsorship or through entrepreneurial efforts of investigators and/or the University; and the relationships between government, academia, industry and others are complex and often legitimately include financial relationships.

Nevertheless, the primary duty of the University, and particularly the IRB, must be to protect the rights and welfare of human subjects while conducting unbiased research.

The University, the IRB and investigators must consider whether specific financial relationships or other considerations create conflicts of interest in research that may bias judgment and affect the rights and welfare of subjects and, if so, to determine what actions must be taken to protect those subjects. In such deliberations, it should be noted that a conflict of interest is not intrinsically wrong, that financial interests of IRB members, investigators and the University and affiliated institutions are not in all cases prohibited, and that not all financial interests have the potential to cause conflicts of interest and thereby to bias judgment and affect the rights and welfare of human subjects.

It is within the discretion of the IRB to decide whether such conflicts of interest are manageable, and if so, to devise a management plan for the protection of human subjects participating in the study.

A conflict of interest creates an ethical problem if a breach of duty or other improper act is caused by the incentive created by the conflict. The key is that the Belmont principles protecting human subjects should not be compromised by financial relationships or other conflicts of interest. Rather, these principles should be maintained by openness and honesty in addressing conflicts. To the extent financial or other conflicts of interest may affect the rights and welfare of human subjects in research, the IRB, institutions and investigators must consider what actions may be necessary to protect those subjects and must ensure the implementation of these actions.
4.2 IRB MEMBERS, ALTERNATE MEMBERS, AD HOC MEMBERS AND GUESTS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: October 27, 2006

IRB members, alternate members and all staff and leaders of the HSRO shall sign an agreement defining that they understand and acknowledge that, as part of their duties or their activities at meetings or in the HSRO office environment, they are bound by the University's conflict of interest policies. This agreement shall also be signed by guests at IRB meetings and by consultants and others who provide input into an IRB review prior to their participation in that review.

Included in these policies is that unless requested by the IRB chair or designee in charge of the meeting, IRB members, alternate members, ad hoc members, guests, HSRO staff, consultants or others may not participate in IRB deliberations of studies with which they, their spouses, or dependent children have a financial or personal interest in the sponsoring agency(s) or other interested parties or for which they may reasonably anticipate future financial benefit or support. Individuals with any of the conflicts defined above may not vote or serve as a reviewer of the study being discussed and may not be counted in the meeting quorum (if applicable). At the request of the IRB Chair or Chair-designee, however, such members or guests may be present at an IRB meeting to answer questions but may not be present during deliberations or voting on the study [45 CFR 46.107(e), 21 CFR 56.107(e)].

"Financial interest" includes but is not necessarily limited to:

1. Salary, consulting fees, honoraria, royalty payments, dividends, loans or other compensation from sponsoring agency(s), other interested parties or individuals with any of the conflicts for services, payments or consideration with value that exceed $10,000 in any preceding 12 month period or in an anticipated 12 month period

2. Serving in a management position such as director, officer, partner or trustee with the sponsoring agency(s), any entity allied with the sponsoring agency(s) or other interested entity

3. Having an ownership interest, equity in the form of stock, stock options or any other investment equal to or exceeding $10,000 (current market value) or a 5% or greater ownership interest in sponsoring agency(s) or any entity allied with the sponsoring agency(s) or other interested entity

4. Having any intellectual property rights such as patents (actual, planned or applied for) or a copyright or license fees or royalties in connection with the technology or product related to the study or the sponsoring agency(s)
IRB members, alternate members, ad hoc members, consultants and guests may not participate in IRB deliberations and they may not vote or serve as a reviewer of studies in which they, their spouses or dependent children serve as Principal Investigator, co-investigator or key personnel. At the request of the IRB Chair or Chair-designee, such individuals may be present at an IRB meeting to answer questions but may not be present during deliberations or voting on the study.

IRB members, alternate members, ad hoc members, consultants and guests are expected to inform the IRB Chair or Chair-designee whenever a conflict of interest is applicable by policies defined above or by reasonable perceptions that financial or other considerations may compromise or have the appearance of compromising the individual's professional judgment and the independence of his/her input into the review process.

In addition, there may be no undue influence by University administrators, Principal Investigators, key personnel or other employees of the University on the selection of IRB reviewers.

Members having any potential conflict of interest regarding the discharging of duties as voting IRB members should:
1. Announce the conflict and recuse themselves from participation during review of that research study except to provide information on request
2. Leave the meeting during the discussion and not vote on any motion to approve or disapprove the study in question

[NOTE: When a person with a conflict of interest leaves the meeting, he/she cannot be counted towards a quorum. If the quorum is lost, the review of the study shall be tabled.]
4.3 PRINCIPAL INVESTIGATORS AND KEY PERSONNEL

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: October 27, 2006

The IRB shall be concerned about the potential for biased judgment and/or other abuse when investigators or study staff have a financial obligation or interest that may pose a conflict of interest which competes with the obligation to protect the rights and welfare of human subjects. The primary goal of this conflict of interest policy is to prevent conflicting interests from adversely affecting the protection of subjects and/or the credibility of the UM human subject protection program if publicly disclosed. The process to manage conflicts of interest (whether real or perceived) shall not vary according to funding source and shall involve three steps:

Conflicts of interest (which may include those of the Principal Investigator, key personnel or the University or affiliated institutions) must be disclosed to the HSRO by the Principal Investigator or any individual listed as "Key Personnel" within the study.

If the conflict exists prior to IRB review of the study, the conflict must be disclosed prior to the IRB deliberation. If the conflict is initiated after IRB review, the conflict must be disclosed to the HSRO within 10 days after its onset.

To ensure the reporting of conflicts in applications for new studies, the IRB shall require that the Principal Investigator and all key personnel, and each member of the faculty and study staff who has contact with potential or consented subjects, disclose, in signed statements within their application, all potential financial conflicts of interest on the part of investigators or institution. With this disclosure, Principal Investigators may recommend to the IRB how the potential conflict of interest should be minimized or resolved.

Among personal financial conflicts of interest that are related to the sponsoring agency(s), any entity allied with the sponsoring agency(s) or other interested entities and that must be disclosed are:

1. Salary, consulting fees, honoraria, royalty payments, dividends, loans or other compensation for services, payments or consideration with value that exceed $10,000 in any preceding 12 month period or in an anticipated 12 month period
2. Serving in a management position such as director, officer, partner or trustee
3. Having an ownership interest, equity in the form of stock, stock options or any other investment equal to or exceeding $10,000 (current market value) or a 5% or greater ownership interest
4. Having any intellectual property rights such as patents (actual, planned or applied for), licensing agreements or a copyright or royalties with the study or the sponsoring agency(s)
5. Having any intellectual property rights not directly involved in the study but that may benefit from the study
Principal Investigators must also recognize that financial conflicts of interest may arise that are not directly related to the Principal Investigator but are related to the University or affiliated institutions. Among such potential conflicts that must be disclosed by the Principal Investigator are:

1. The research involves a drug, device or other invention created at the University or affiliated institution or by an employee currently or formally at the University or affiliated institution who is not the Principal Investigator or key personnel of the study.
2. The research involves a drug, device or other invention created by someone other than the Principal Investigator or key personnel for which the University or affiliated institution holds a financial interest and/or may derive financial benefit.
3. The research involves a drug, device or other invention for which someone who is a colleague of the Principal Investigator or key personnel is creator and/or holds a financial interest.
4.4 Human Subject Conflict of Interest Committee

Review Responsibility: IRB Policy and Procedure Committee  
Current Approval Date: October 27, 2006

A Human Subject Conflict of Interest (HSCOI) Committee has been constituted to review and make recommendations on conflicts of interest. This Committee shall be composed of the chairs and vice-chairs of the UM IRB panels with the exception of the chairs and vice-chairs of panels employed by an extramural, commercial IRB. Membership on this committee shall also include a community representative and the Assistant Provost for IRB Affairs who shall chair this Committee. This membership structure shall enhance consistency among the UM IRB panels with regard to managing conflicts of interest.

Information about conflicts of interest shall be provided by Principal Investigators to the HSRO for forwarding to the members of the Human Subject Conflict of Interest Committee. HSCOI Committee members may make individual recommendations directly to the Committee chair or, if one or more members so request, the Committee shall be convened in a meeting to deliberate and make recommendations on the matter. The Committee chair is responsible for summarizing Committee recommendations and for forwarding this summary and individual written statements if submitted by committee members, to the IRB for its deliberations.

The HSCOI Committee may not suspend an on-going study or disapprove a study undergoing initial review. Rather, the HSCOI may make such recommendations as it believes appropriate to the IRB.

If the putative conflict of interest is disclosed after IRB approval of a study and that study has not yet commenced and no subjects have been enrolled, the Principal Investigator may voluntarily suspend enrollment and the putative conflict of interest shall be reviewed in the same manner as for new studies (i.e. the Human Subject Conflict of Interest Committee shall make recommendations to the IRB and the IRB shall deliberate on the management of the conflict (see below).

If the putative conflict of interest is disclosed after IRB approval of a study and subjects have been enrolled, the information shall be forwarded by the HSRO to the HSCOI in a timely manner both to provide the IRB with recommendations on conflict management and also for a recommendation as to whether the conflict poses additional risk to subjects. If the Committee believes that risk to subject is increased by the conflict in a manner that requires immediate suspension of the study until the conflict is managed, this recommendation shall be forwarded to the Associate Vice Provost for Human Subject Research who may suspend the study pending IRB review.
4.5 IRB REVIEW AND APPROVAL OF CONFLICT MANAGEMENT

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: October 27, 2006

If a conflict of interest is reported to the IRB prior to its approval of the study, the IRB shall deliberate upon the conflict and resolve its management as a criterion for approval of the study. If a conflict of interest is reported to the IRB after approval of a study, the IRB shall deliberate upon the conflict and resolve its management as a criterion for permitting continuance of the study.

A key to IRB determinations shall be the IRB evaluation as to whether the conflicts could challenge, or be perceived by others to challenge, the integrity of a reasonable individual or the institution itself, whether the conflicts could result in decisions that adversely affect the production of valid scientific results and whether the conflicts might adversely affect the protection of human subjects or the credibility of the human research protection program. It shall then be the responsibility of the IRB to determine if the institution is an appropriate site for the research, whether the research should be approved and whether (and how) the conflicts shall be managed or eliminated so they no longer affect the protection of human subjects or the credibility of the human research protection program.

The IRB will determine whether the conflict is permissible in the context of the protocol or whether additional actions must be taken. Such actions may include (but are not limited to):

1. Requiring partial or complete financial divestiture
2. Requiring an independent investigator to obtain consent or conduct the research
3. Requiring an independent data safety monitoring committee or similar monitoring body
4. Requiring additional oversight or monitoring of the research
5. Requiring a second or parallel site for the study
6. Requiring modification of the role(s) of particular research staff, changes in location for certain activities or prohibition of UM as a study site
7. Requiring frequent continuing review
8. Requiring separation of responsibilities for financial decisions and research decisions
9. Requiring that additional information be given to subjects as part of the informed consent process if, in the IRB’s judgment, the information would meaningfully add to protection of the rights and welfare of subjects [45 CFR 46.109(b), 21 CFR 56.109(b)]
10. Disapproval of the study
SECTION 5: INSTITUTIONAL REVIEW BOARDS
5.1 IRB Membership and Structure

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: July 1, 2008
Revised: May 24, 2011; June 8, 2011

Each of the UM Institutional Review Boards is a fully functioning, standing committee, which is independent of any other committee at the University or JHS. As assigned by the HSRO, each IRB shall review human subject research studies that fit (entirely or in part) any of the following:

1. The studies are conducted by employees or students of UM, JHS or affiliates
2. The studies are conducted on UM or JHS premises
3. The studies utilize UM or JHS facilities or resources
4. The studies are conducted at non-UM or JHS sites but UM or JHS personnel are engaged in the research in connection with their institutional responsibilities.

Studies will be assigned to an IRB by staff members of the HSRO who serve as designees of the Associate Vice Provost for Human Subject Research. These assignments will be made by trained HSRO staff according to the expertise of IRB members and their workload pursuant to the recommendations and guidance of the Assistant Provost for IRB Affairs and the chairs of each IRB.

Selection of an IRB panel by an investigator shall not be permitted; but an IRB Chair or IRB-designee, at his/her discretion, may recommend to the HSRO that the review of a research study be referred to another IRB panel if he/she determines that another IRB panel has more appropriate expertise or if IRB meeting schedules make the transfer appropriate. Upon such recommendation, the Associate Vice Provost for Human Subject Research or, in his/her absence, the Assistant Provost for IRB Affairs shall make the final decision on the IRB assignment.

Once an IRB has approved a study, all additional oversight and actions shall typically be performed by that same panel (i.e., continuing review, expedited review, and adverse event considerations). Each IRB is distinct and completely separate from the other IRBs. If an issue affects more than one IRB (e.g., an investigator with studies open under more than one IRB is failing to comply with regulations), each IRB may address the issue separately or together, under the coordinating assistance of the Associate Vice Provost for Human Subject Research or the Assistant Provost for IRB Affairs.

Each IRB should include individuals with a broad range of expertise who are qualified to review the research through their education, experience, expertise and diversity. All appointments to an IRB shall be reported to the Office for Human Research Protections (OHRP). The IRB roster shall identify the primary member(s) for whom each alternate member may substitute. The qualifications of each alternate member must be comparable to those of the primary member to be replaced. Alternate members are invited to attend IRB meetings and may participate in discussions but may vote only when
replacing a voting member of the IRB. When an alternate member replaces the primary member, the alternate member shall receive and review the same material that the primary member received. IRB meeting minutes shall document instances in which an alternate member replaces a primary member.

Each UM IRB shall have at least five members including at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. During the review of FDA-regulated products (drugs, biologics, and devices) at least one member present must be a licensed physician. A priority shall be placed on diversity of IRB membership, including race, gender, cultural backgrounds, sensitivity to community issues and community attitudes, and multiple professions representing the scope of research under IRB review. Priorities shall also be on having both sufficient lay (non-affiliated) representation to reflect the values of the community from which the research subjects are drawn and members with broad, scientific expertise.

At least one member of each IRB shall not otherwise be affiliated with the University of Miami or Jackson Health System and may not be part of the immediate family of a person so affiliated. Members of the community such as clergy, teachers, attorneys, veterans or representatives of legally-recognized veterans organizations, and community and/or prisoner advocates shall be considered for appointments to the IRB. One IRB member may fulfill both criteria of non-scientist and non-affiliate at the same meeting.

IRB members should be committed to safeguarding the rights and welfare of human subjects. Members who do not adequately fulfill their responsibilities as judged by the IRB Chair, the Assistant Provost for IRB Affairs and/or the Associate Vice Provost for Human Subject Research may be relieved from IRB membership by the Associate Vice Provost for Human Subject Research.

Compensation may be provided to IRB members who are employees of the University of Miami in the form of salary support for service related to duties. Such compensation may be provided if the IRB duties constitute a significant fraction of the member's time and if compensation for that time is not otherwise provided from institutional and/or department or other resources. The Associate Vice Provost for Human Subject Research shall manage compensation standards for such services.

When acting in accordance with federal, state, and local regulations and the UM IRB Written Policies and Procedures, IRB member actions are covered by the University's self-insurance policy, which protects individuals from liability when performing within the course and scope of their IRB responsibilities and in accord with faculty and staff serving on all University Boards or Committees. Unaffiliated members of the IRB are also covered by this policy when performing within the course and scope of their IRB service.

The Associate Vice Provost for Human Subject Research and/or the Assistant Provost for IRB Affairs and/or the IRB chairperson may, at his/her discretion, recruit non-voting (ad-hoc) members to the IRB from among the academic or administrative staff of the University, whose presence at the meetings of the IRB would aid the IRB in conducting its duties. These ad-hoc members may take part in IRB meetings, participate in the discussions and make recommendations to influence decisions, but they
may not vote on the decisions. Non-voting members shall not be included in determining or establishing a quorum at the meetings. IRB meeting minutes shall reflect the presence of non-voting members.

Each IRB is charged with evaluating the scientific merit when participants will be placed at more than minimal risk, determining risk-benefit ratio, and assessing the ethical and legal aspects of each project. These functions, operations, reviews, and requirements are in accordance with the requirements of 45 CFR 46 and FDA Parts 50 and 56.

The number and scope of IRBs shall be defined by the Associate Vice Provost for Human Subject Research based on evaluations of the thoroughness and timeliness of IRB actions. Determination of the appropriate number of IRBs shall take into account the volume, complexity and types of research reviewed, and the time/effort IRB members devote to IRB activities, given other responsibilities.
5.2 IRB CHAIRS AND VICE-CHAIRS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: July 1, 2008
Revised: May 24, 2011

5.2(a) APPOINTMENT OF IRB CHAIRS AND VICE-CHAIRS

Based on candidate interviews and recommendations from institutional leaders including relevant academic department chairs, the Associate Vice Provost for Human Subject Research shall appoint the IRB Chairs with the advice of the Assistant Provost for IRB Affairs. The Associate Vice Provost for Human Subject Research shall appoint the IRB Vice-Chairs with the advice of the Assistant Provost for IRB Affairs and the IRB Chair of the panel that the Vice-Chair will serve. IRB Chairs shall appoint their IRB-designees and administrative-designees.

IRB Chairs and Vice Chairs serve as voting members of the IRB and, as for all members; they must have the knowledge, skills and abilities necessary to carry out the functions of the IRB. In addition, IRB members who serve as Chairs or Vice Chairs must have the leadership and administrative skills necessary to conduct meetings and to exercise the authorities and responsibilities of their positions. Such individuals must also be highly motivated to fulfill the duties of IRB Chairs and Vice-Chairs with the commitment of time/effort necessary for these essential functions.

IRB Chairs and Vice-Chairs will be appointed to one-year terms and are eligible for reappointment at one-year intervals. During the appointment period, an IRB Chair or Vice-Chair may be removed at the discretion of the Associate Vice Provost for Human Subject Research. At least annually during each appointment year, the Associate Vice Provost for Human Subject Research shall decide upon reappointment with the advice of the Assistant Provost for IRB Affairs. This decision shall be based on the policy and criteria for appointment of IRB members (c.f. Section 5.3A) and upon review of the leadership and administrative performance of each IRB Chair and Vice Chair, on relevant information sought as deemed necessary from IRB members, HSRO staff and others, on review of IRB minutes and determinations and on performance review meetings with each Chair and Vice Chair.

In addition to their authorities and responsibilities as IRB Chairs and Vice-Chairs, such individuals serve as members of the IRB and are counted for the quorum. They shall have voting privileges and other authorities and responsibilities of members including the responsibility to review, make motions, participate in discussions and vote on approval/disapproval of studies.
5.2(B) AUTHORITIES AND RESPONSIBILITIES OF IRB CHAIRS AND VICE-CHAIRS

Responsibilities of the IRB Chair include but are not limited to those defined in the following three sections. In the absence of the IRB Chair, the Vice-Chair shall assume the responsibilities of the IRB Chair. In the absence of both the IRB Chair and Vice-Chair, the IRB Chair may appoint an IRB member to assume the responsibilities of the IRB Chair.

1. Ongoing IRB Chair Responsibilities:
   a. Review and approve, when appropriate, expedited submissions in accordance with regulatory requirements
   b. Determine exempt submissions in accordance with regulatory requirements
   c. Review (or defer to the primary reviewer or other IRB-designee to review) all on-site serious adverse event reports (SAEs) and unexpected problems affecting the safety of subjects and, as necessary, determine if one or more of the following is necessary:
      · Immediate action to address the safety of subjects
      · Call an emergency meeting of the IRB
   d. Appoint qualified IRB members as IRB-designees with authority for expedited reviews and other actions as defined in these Policies and Procedures
   e. Appoint qualified HSRO staff members as administrative-designees with review and signature authority as defined in these Policies and Procedures
   f. Maintain a thorough understanding of federal regulations pertaining to human subject protections, the UM IRB Written Policies and Procedures, and other applicable state, and local regulations. Assure that regulations and policies are applied in all IRB matters with a commitment to foster ethically and scientifically sound human subject research
   g. Respect the diverse backgrounds, perspectives and sources of expertise of all IRB members and foster such respect among the IRB members
   h. Uphold IRB judgments no matter how these are received or perceived by Principal Investigators

2. IRB Chair Responsibilities Prior to Each Convened Meeting:
   a. Review IRB meeting schedule and agenda composed by the HSRO
   b. Ensure coverage by the Vice-Chair when not able to serve as Chairperson for the meeting and notify the HSRO when not able to serve
   c. Provide guidance to the HSRO on the assignment of reviewers to studies requiring convened IRB review
   d. Assist the IRB reviewers and other IRB members with any concerns in preparing for the meeting, as necessary
   e. Recommended consults when appropriate to assist in IRB reviews

3. IRB Chair Responsibilities during IRB Meetings:
a. Preside over IRB meetings and ensure that meetings are conducted in an efficient, orderly and fair manner with respect given to the opinions of all members. Robert's Rules of Order should be used as a guidebook for conducting the meeting.
b. Ensure a quorum for each study review and ensure that this quorum is properly documented.
c. Ensure that all regulatory-required elements of review are addressed during the meeting and that there is meaningful and substantive discussion of relevant matters and/or questions.
d. Ensure that assigned reviewers present a clear and concise review of study materials including consent documents and recruitment items and process
e. Ensure that all IRB-required changes to consent and other documents are documented
f. Ensure that the IRB discusses specific findings, as required by regulations, whenever these is the involvement of vulnerable populations, e.g. children, prisoners, pregnant women and fetuses
g. Accept appropriate motions from voting members of the IRB.
h. As necessary, ensure that the specific elements pertaining to the motion are clearly understood by the IRB and accurately recorded in the meeting minutes
i. Ensure that IRB decisions are made in accordance with federal, state and local regulations and with the UM IRB Written Policies and Procedures
j. Ensure that minutes of IRB meetings and votes of the IRB members accurately reflect discussions and actions
5.3 IRB MEMBERS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: July 1, 2008
Revised: May 24, 2011; June 8, 2011

5.3(A) APPOINTMENT OF IRB MEMBERS

The Associate Vice Provost for Human Subject Research shall appoint IRB members and alternate members with the advice of the Assistant Provost for IRB Affairs. These appointments shall be based on candidate interviews, recommendations from institutional leaders and others including relevant academic department and IRB chairs, review of the candidate’s expertise, qualifications and accomplishments as demonstrated in his/her curriculum vitae and other academic documents deemed relevant, and pursuant to the needs for expertise within IRB panels.

IRB members and alternate members shall be appointed to one-year terms and are eligible for reappointment at one-year intervals. During the appointment period, an IRB member or alternate member may be removed at the discretion of the Associate Vice Provost for Human Subject Research. At least annually during each appointment year, the Associate Vice Provost for Human Subject Research shall decide upon reappointment with the advice of the Assistant Provost for IRB Affairs. This decision shall be based on recommendations from the IRB Chair and other relevant information sought as deemed necessary from IRB members, HSRO staff and others, and on review of IRB minutes. Additional criteria of satisfactory performance for the continuance of IRB member and alternate member appointments, and for their reappointment, shall include attendance at meetings and training sessions, success in required training and education, meeting preparation, professionalism in the review process, and diligence in accomplishing the needs of the IRB and the HSRO for timely and appropriate review and decision-making of all assigned research studies.

5.3(B) AUTHORITIES AND RESPONSIBILITIES OF IRB MEMBERS AND ALTERNATE MEMBERS

IRB members and alternate members are appointed to serve the University of Miami and affiliated institutions as a whole. Members and alternate members must put their duty to protect the rights and welfare of human subjects above their own interest or that of their academic department.

IRB members are responsible for attending, for their full duration, all convened IRB meetings in a timely manner. If an IRB member cannot attend a meeting or a part of a meeting, he/she should notify the HSRO well in advance of the meeting to facilitate the preparation and attendance of an appropriate alternate IRB member.
All IRB members and alternate members should understand and apply the ethical principles of the Belmont Report and all federal, state and local regulations related to the protection of human research participants. Members and alternates should commit time and effort to receive training in these requirements. All members and alternate members shall be given copies of pertinent documents to review and understand including federal regulations and the University of Miami’s Written Policies and Procedures for the Protection of Human Subjects in Research. Attendance at University of Miami seminars pertaining to human subject protections is encouraged. These seminars are intended to provide background and new information. In addition, IRB members and alternates are encouraged to attend relevant local and national meetings and may be provided support to do so.

IRB members (and alternate members when appropriate) are expected to serve as primary reviewers for assigned studies and to participate as general reviewers on all studies discussed at convened meetings. IRB members (and alternate members when appropriate) shall vote to approve, set conditions for approval, defer review to expedited reviewer or convened IRB or disapprove studies submitted to the IRB following discussion of these studies. IRB members (and alternate members when appropriate) may discuss and vote on other matters pursuant to UM Policies and Procedures such as compliance audit reports or reports of adverse events.

IRB members may be appointed as IRB-designees by the IRB Chair or Vice-Chair. IRB-designees are expected to conduct exempt and expedited reviews.

5.3(c) Administrative-Designees
Upon recommendation of the Associate Vice Provost for Human Subject Research, the IRB Chair may appoint trained administrative staff members of the Human Subject Research Office as administrative-designees of the IRB. Administrative-designees have specific review and approval authority that is defined in other sections of these Policies and Procedures. These responsibilities are limited to such matters as non-human subject research, final reports and informational amendments.
SECTION 6: IRB MEETINGS
6.1 AGENDA

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 14, 2006
Revised: May 24, 2011

Convened meetings of an IRB shall have an agenda, constructed by HSRO staff, which clearly shows the topics and items that the members will consider at the meeting. The agenda shall identify each study by title, UM IRB number and Principal Investigator name. Agendas shall be considered a "tool" utilized by the HSRO and IRB to assist in the organization and conduct of meetings and in preparation of minutes. Agendas will become part of the official meeting record to assist location of a specific item or action in the minutes of the meeting.

Examples of agenda items include:
- Review of previous meeting minutes
- Discussion items
- Staff Reports
- Reports of Unanticipated Problems and Adverse Events
- Reports of Changes in Research (Amendments)
- New studies submitted for review
- On-going studies submitted for continuing review
- Reports of expedited and exempt reviews
- Exempt Reviews
- Audit Reports
- Educational sessions and materials
6.2 MINUTES

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 14, 2006
Review: May 24, 2011; June 8, 2011

It is the responsibility of the HSRO to ensure that official IRB meeting minutes, recording the reviews, deliberations and votes of the IRB are written and subsequently provided to the IRB for approval. If applicable, these minutes should be in sufficient detail to demonstrate that the review of studies, modifications, unexpected events and continuing reviews were done in accordance with federal, state and local laws and regulations and with university policies and that the safety and welfare of human subjects are protected.

It is also the responsibility of the HSRO to make any corrections to the minutes as defined by the IRB. IRB votes to approve, disapprove, defer or table studies or other matters shall be recorded. If an IRB member elects to abstain from a vote, the minutes shall record the abstention. Minutes shall not reflect how an individual member has voted on any particular motion but shall reflect only the outcomes of voting actions.

Required information to be documented within meeting minutes relative to IRB reviews and decision is defined in federal regulations [45 CFR 46.115(a)(2) and 21 CFR 56.115(a)(2)]. This information shall include but is not limited to:

1. Attendance at the start of the meeting, the mode of attendance if other than in person (i.e. video conference, teleconference, etc.) and any changes in attendance or the mode of attendance that occur during the meeting
2. Documentation that all members received all pertinent materials prior to the meeting and were able to actively and equally participate in discussions
3. The presence of a quorum throughout the meeting including the presence of at least one member whose primary concern is in a non-scientific area, the presence of at least one member not affiliated with the university and the presence (if applicable) of consultants with the appropriate expertise to provide guidance/recommendations to the IRB upon request of the IRB
4. The review and approval of previous meeting minutes
5. That any IRB member with a real or potential conflict of interest relative to a study under consideration was not present during the deliberations or voting on the proposal (and that the quorum was maintained)
6. The determination of the level of risk in each reviewed study
7. The determination of the risk level of an investigational device (if applicable) and the rationale for this determination
8. The determination of whether or not the subject population will receive any direct benefit or if there is benefit to society as a whole
9. The deliberations (if applicable) on the justification for waiving any or all of the required elements of informed consent
10. The determination that informed consent documents were reviewed in accordance with applicable regulations and contains all of the required elements
11. Actions taken by the IRB
12. The vote on actions taken by the IRB including the number of members voting for, against and abstaining
13. The basis for requiring changes in or disapproving studies and documentation of resolution of these issues if/when resolution occurs
14. The length of time of an approval
15. A written summary of the discussion with emphasis upon the identification and deliberation related to controverted issues and the resolution of such issues
16. The deliberations relevant to the inclusion and safeguarding of vulnerable populations if entered as study subjects
17. Documentation of the required findings when approving a consent procedure that does not include or that alters some or all of the required elements of informed consent or when waiving the requirement to obtain an informed consent or when waiving the requirement to obtain documentation of informed consent
18. Any educational/training information provided to the IRB during the convened meeting

In addition to the review of pending studies, meeting minutes shall include (when applicable) a summary and other relevant information regarding expedited approvals, modifications, terminations, emergency/single patient use, placebos, symptom provocation, adverse events and unanticipated problems, and any other business appropriate for IRB meetings.

Minutes shall be included on the agenda of a subsequent IRB meeting and be available for approval by the IRB. Once approved, the minutes shall not be altered. The minutes of the IRB meetings shall be maintained in the HSRO office for a minimum of three (3) years following closure of each study discussed at the meeting covered by the minutes.

Upon request, any IRB member shall have access to the complete IRB study file and relevant IRB minutes prior to or during the convened IRB meeting.
6.3 REVIEWER ASSIGNMENTS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 14, 2006
Revised: May 24, 2011; June 8, 2011

The IRB Chair, IRB-designee of the chair or an HSRO Administrator assigned to that IRB may designate IRB members as the Primary or Secondary Reviewers for a study to be reviewed by the IRB. Both the primary and secondary reviewers should have sufficient expertise to adequately fulfill these roles. If an IRB member believes that he/she cannot be a reviewer for a particular study for any reason, including but not limited to a lack of expertise or to a conflict of interest, the IRB Chair or the HSRO Administrator should be immediately notified.

Both the Primary and Secondary Reviewers should carefully review all aspects of the submission, including the protocol, consent form, and other accompanying materials. If the Primary Reviewer is unable to present a summary and recommendations for a submission due to absence, the Secondary Reviewer will be expected to do so. If the IRB finds that its membership lacks sufficient expertise to appropriately review a specific study, it may seek additional expertise outside of the membership of the IRB. Individuals invited to assist in reviews of issues that require expertise beyond or in addition to that available on the IRB may participate in discussions but may not vote with the IRB.

Assignments to primary and secondary reviewers notwithstanding, all IRB members shall be provided with the required materials to ensure thorough initial and continuing review of each research matter. The entire IRB file shall be available to all IRB members prior to and during the convened meeting, and all IRB members shall be afforded full opportunity to discuss each research matter during the convened meeting.
6.4 CONSULTANTS AND AD HOC REVIEWERS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 14, 2006
Revised: May 24, 2011; June 8, 2011

Although IRB members are encouraged to seek informal consultation as a normal part of their review process, care should be given regarding confidentiality issues.

At its discretion, the IRB may invite scientists or non-scientists from within or outside the University, who have special expertise, to function as consultants and ad hoc reviewers of human research studies. Once a consultant is identified, s/he shall be provided with a confidentiality agreement for signature, and must affirm that s/he has no conflict of interest pursuant to University policy or individual sponsor contact. Contingent upon receipt of the signed confidentiality agreement and the conflict of interest affirmation by the HSRO, the consultant shall be provided with all documents submitted to the IRB relevant to the specific matters under IRB review as well as the questions posed by the IRB for which guidance is being sought.

Guidance/recommendations to the IRB from consultants may be given by personal contact, in writing, by phone, through the internet or other appropriate communication mechanisms. Verbal guidance/recommendations from consultants provided to the IRB chair or designee conducting expedited reviews shall be summarized by the IRB chair or designee and included within the study file. Written guidance/recommendations from consultants provided to the IRB chair or designee conducting expedited reviews shall be added to the study file. Verbal or written guidance/recommendations from consultants provided to the convened IRB shall be presented at the IRB meeting by the member or other receiving entity and summarized in the meeting minutes. If in writing, such guidance/recommendations from consultants shall be added to the study file.

A consultant may advise in the preparation of a presentation to the IRB, may participate at the deliberations as a guest at the request of the IRB and may make recommendations on the project, but s/he may not vote.

If an IRB member believes that a consultation is required, s/he may identify the consultant and recommend consulting fees to the Associate Vice Provost for Human Subject Research, who is authorized to determine and arrange for reasonable compensation to consultants.
6.5 CONFIDENTIALITY OF IRB MEETINGS AND GUEST POLICY

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** March 14, 2006  
**Revised:** May 24, 2011

Proceedings of IRB meetings are considered confidential. IRB members, alternate members and ex officio members should not disclose information about studies including (but not limited to) contents of files, details of discussions and the attribution of comments to specific committee members. Such members must sign IRB confidentiality agreements.

Persons may be permitted to attend UM IRB meetings as guests under the following conditions:
1. Guest attendance is at the discretion of the IRB chair or IRB-designee  
2. Guests may be asked to leave at any time  
3. Guests may not be in attendance during the deliberations relative to a study in which they serve as PI, co-investigator or key personnel  
4. Guests must sign a confidentiality agreement  
5. Guests must reveal any conflicts of interest prior to attendance and/or must excuse themselves if a potential conflict reveals itself  
6. Guests shall sign in and may be asked to document the purpose of their visit
6.6 **MEETINGS AND QUORUM**

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** March 14, 2006  
**Revised:** May 24, 2011

A goal to assure the effectiveness of the review process shall be to schedule IRB meetings at least once every other week. The HSRO shall ensure that meetings are scheduled in advance and that an agenda and all pertinent documents are made available to members (and alternates if appropriate) with sufficient time prior to meetings. Individual meetings may be cancelled by the Associate Vice Provost for Human Subject Research or the Assistant Provost for IRB Affairs following consultation with the IRB Chair due to:

1. Insufficient applications or other matters requiring convened board review
2. University holiday
3. Inability to secure a quorum for attendance
4. Other reasons (such as inclement weather) that make a scheduled meeting unnecessary or otherwise inappropriate

Except when an exempt or expedited review procedure is used, the IRB shall review initial or continuing studies at a convened meeting at which a quorum is present. A quorum for a convened IRB meeting is 50% of the voting primary membership (including alternate members who may replace voting members) plus one. A quorum must be maintained for each vote to occur. If a quorum is not maintained, the meeting shall end or be suspended and any remaining items shall be tabled.

Additional quorum policies are:

1. The IRB chair and vice chair count toward the quorum
2. At least one member whose primary concerns are in nonscientific areas must be present to complete a quorum
3. If research involving an FDA-regulated article is involved, a licensed physician must be included in the quorum
4. Members absenting themselves due to conflicts of interest may not be counted toward quorum requirements

Although the physical presence of IRB members at meetings is encouraged, a member or alternate member (if appropriate) may be considered present if participating through teleconferencing or videoconferencing. In this case, the member or alternate member must have received all pertinent material prior to the meeting and must be able to participate actively and equally in all discussions and votes. Minutes of such meetings shall clearly document that these two conditions have been satisfied in addition to the usual regulatory requirements.
6.7 VOTING

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 14, 2006
Revised: May 24, 2011; June 8, 2011

Robert’s Rules of Order\(^1\) is the standard used to guide IRB interactions and decisions. At a minimum, the Chair conducts the meeting, there is a pre-determined agenda, the minutes of the prior meeting are voted upon, and all actions and resolutions require a vote by voice (if a member is participating through teleconferencing or videoconferencing) or show-of-hands vote of the members present following discussion and the making and seconding of a motion.

The IRB Chair and Vice Chair are voting members of the IRB and their presence counts towards the quorum. The official meeting minutes record shall define the number of votes to approve, disapprove, defer or table without identifying the IRB member who cast that vote. The official meeting minutes shall also define the number of votes cast as abstentions. In the event an IRB member elects to abstain, the minutes shall record the abstention.
SECTION 7: GENERAL PRINCIPLES FOR IRB REVIEWS
7.1 SUBMISSION OF NEW OR CONTINUING STUDIES

Review Responsibility: IRB Policy and Procedure Committee  
Current Approval Date: March 14, 2006  
Revised: May 24, 2011

Documents and necessary forms required for substantive and meaningful IRB review of new or continuing studies shall be submitted by the Principal Investigator to the HSRO through its computer system (ePROST).

The HSRO shall screen submitted documents and forms for completeness before assigning the study to the appropriate IRB. If the application is found to be incomplete or otherwise not fully prepared for IRB review, it shall be returned to the Principal Investigator or a request shall be made for necessary changes or to provide additional information. The HSRO or an IRB member may contact the Principal Investigator to request clarification of study issues or revisions in document(s) prior to review by the IRB or during the review process.
7.2 RECOMMENDATIONS FOR REVIEW CATEGORY

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 14, 2006
Revised: May 24, 2011

As part of the submission process for new or continuing studies, the Principal Investigator shall be asked to recommend whether the study, by its scope and protocol, falls into one of the specific review categories defined in 45 CFR 46 and 21 CFR 56. These categories are:

1) Exempt Review (does not apply to studies regulated by the FDA)
2) Expedited Review
3) Convened IRB Review

It is the responsibility of the Principal Investigator to understand and request an appropriate review category for his/her application. Investigators are urged to consult with HSRO regulatory staff before making their recommendations to the HSRO and the IRB regarding the review category.

The submissions and recommendations by the Principal Investigator are made to the HSRO where they are screened by trained HSRO staff who shall forward the recommendations of Principal Investigators and the recommendations made by them (the staff) on behalf of the HSRO to the IRB. Final decisions as to the review category of new or continuing studies shall be made by the IRB.

The HSRO recommends and the IRB determines review category on the basis of federal regulations and the guidance provided on the website of the Office for Human Research Protections (OHRP). Specific information on determining the review category for study applications is provided in subsequent sections of these policies.

Those studies recommended and meeting criteria for exempt or expedited review shall be forwarded to the IRB chair or chair-designee for review. Chair-designees must be members or alternate members of the IRB. The IRB chair or chair-designee shall make the final decision as to whether the study may be reviewed within the proposed exempt or expedited category or whether the study should be deferred to the convened IRB.

IRB chairs and chair-designees shall conduct reviews of studies that fit within the exempt or expedited categories on behalf of the IRB. The applications of those studies that fit under the "Convened IRB Review" category shall be made available to all members of the IRB. IRB chairs/IRB-designees may determine that studies recommended for exempt or expedited review require convened IRB review. Conversely, the convened IRB may determine that studies recommended for "Convened IRB Review" require exempt or expedited review.
7.3 CRITERIA FOR IRB APPROVAL

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: June 5, 2007
Revised: May 24, 2011

The IRB chairs, IRB-designees and convened IRB shall conduct a systematic review of the study materials and shall consider the same principles and criteria in its deliberations of all new or continuing studies, no matter whether these fall into the exempt, expedited or convened IRB category, in accordance with 45 CFR 46 and 21 CFR 56. Among these criteria are:

1) Research Relevance.  
2) Minimization of Risks. Both physical and non-physical risks to human subjects should be minimized to the extent possible by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk. Whenever appropriate, studies should use procedures already being performed on the subjects for diagnostic or treatment purposes (45 CFR 46.111 and 21 CFR 56.111).
3) Reasonable Risk/Benefit Ratio. Both physical and non-physical risks to human subjects should be reasonable in relation to any anticipated benefits (the risk/benefit ratio) to subjects, and the importance of the knowledge that may reasonably be expected to result. The IRB should account for risks and benefits that may result from the research as distinguished from those that subjects would receive if not participating in the research. The IRB should not consider possible long-range effects of applying knowledge obtained in the research. The IRB should take into consideration the level of risk and the validity of the research design in determining the risk/benefit ratio (45 CFR 46.111 and 21 CFR 56.111).
4) Equitable Selection of Subjects. The IRB should take into account the research purposes and settings, special problems involving vulnerable populations (e.g. children, prisoners, pregnant women, persons with mental disabilities or impaired decision-making capacity and persons disadvantaged economically or educationally) in evaluating subject selection equities (45 CFR 46.111 and 21 CFR 56.111).
5) Quality Informed Consent Forms. These should contain all required elements, conform with regulations and ethical standards, be complete, accurate and comprehensible and provide potential subjects with an accurate and fair description of the risks or discomforts and the anticipated benefits.
6) Adequate Safety Monitoring and Provisions for Privacy and Confidentiality. The IRB should ensure that research plans make adequate provisions for data and safety-monitoring to protect the privacy of subjects and to maintain the confidentiality of individually-identifiable data (45 CFR 46.111 and 21 CFR 56.111).
7) **Protection of Vulnerable Subjects.** The IRB should ensure that adequate safeguards have been included in each study to protect the rights and welfare of vulnerable subjects (45 CFR 46.111 and 21 CFR 56.111).

8) **Conflict of Interest.** The IRB should ensure that steps are adequate to evaluate, manage, reduce or eliminate potential or real conflicts of interest.

9) **Investigator's Educational Requirements and Certification.** The IRB should ensure that the PI and all personnel engaged in the study have met current educational requirements for the protection of human research subjects as mandated by the University. The IRB should also determine that investigators are qualified through education, training and experience to conduct the research.

The assessment of risks and benefits requires that the IRB carefully and systematically review relevant data including putative alternate ways of obtaining the benefits sought in the research. In conducting its reviews, therefore, all IRB members should receive and review the study application and all supplemental documents (and for continuing reviews, a status report on the progress of the research) and other information (if applicable) including:

1) The number of subjects accrued or to be accrued
2) A summary of adverse events and any unanticipated problems involving risks to subjects or others and any withdrawal of subjects from the research or complaints about the research since the last IRB review
3) A summary of any relevant recent literature, interim findings, and amendments or modifications to the research since the last review
4) Any relevant multi-center trial reports
5) Any other relevant information, especially information about risks associated with the research
6) A copy of the proposed or current informed consent document and any newly proposed consent document

In assessing risks and benefits and the justifiability of research, the IRB shall follow the following five guidelines of the National Institutes of Health (http://ohsr.od.nih.gov/guidelines/Belmont.html):

1) Brutal or inhumane treatment of human subjects is never morally justified
2) Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is necessary to use human subjects at all and/or whether alternative procedures could reduce or eliminate risks
3) When research involves significant risk of serious impairment, the IRB should require written justification of the risk (looking usually to the likelihood of benefit to the subjects – or, in some rare cases, to the discernable voluntariness of the participation
4) When vulnerable populations are involved in research, the appropriateness of involving them should be demonstrated. Variables which should go into such judgments include the nature and degree of risk, the condition of the particular population involved, and the nature and level of the anticipated benefits
5) Relevant risks and benefits must be thoroughly defined in documents and procedures used in the informed consent process.
7.4 APPROVAL DURATION

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 14, 2006
Revised: May 24, 2011

The following shall apply almost exclusively to studies approved under the convened IRB category since studies approved under the expedited category should involve no greater than minimal risk to human subjects and will likely require continuing review only on an annual basis. However, IRB chairs or chair-designees may impose shorter continuing review durations for expedited studies if appropriate.

Federal regulations [45 CFR 46.109(e) and 21 CFR 56.109(f)] require that continuing review of research be conducted by the IRB at intervals appropriate to the degree of risk and not less than once per year. Pursuant to regulations, the IRB shall define the duration of approval of each study with the requirement that all studies, no matter whether previously approved under the expedited or convened IRB review category, shall be subject to continuing review at intervals appropriate to the degree of risk and not less than once per year. Regulations make no provision for any grace period extending the conduct of the study beyond the expiration date of IRB approval.

For studies reviewed and approved by the IRB chair or designee within the "expedited" category, the length of approval shall be calculated from the date that the IRB chair or designee finalized his/her approval. For studies that did not fit within the expedited category and therefore require review by the convened IRB, the length of approval shall be calculated from the date of the convened IRB review at which approval was given. Additionally, where the convened IRB specifies conditions for approval of a study and defers approval until the satisfaction of its conditions are verified by the IRB chair or designee, continuing review must occur no more than one year after the date the study was reviewed by the convened IRB, not on the anniversary of the date on which the IRB chair or designee verifies that IRB-specified conditions for approval have been satisfied.

The approval duration shall be based on evaluations as to whether the risks are of a sufficient magnitude that annual review is inadequate. Although the magnitude of the risks is in part determined by the study procedures, other factors that pertain to the study (e.g., age of participants) may also be considered.
Among the factors that the IRB shall consider in determine whether a study requires continuing review by the IRB more frequently than annually are:

1) If the study involves experimental therapies or procedures in which a clear potential for significant adverse experiences has been identified at the time of review
2) The nature, probability and magnitude of anticipated risks to subjects
3) Likely medical or psychological condition of the proposed subjects
4) Qualifications of the PI and other members of the research team
5) Nature and frequency of adverse events observed in similar research
6) Vulnerability of the population being studied including familiarity with the language on consent forms and other documents
7) Other facts the IRB deems relevant
7.5 PROJECT VERIFICATION FROM OUTSIDE SOURCES

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: August 27, 2007
Revised: May 24, 2011

It is usual that the IRB will make its determinations based on information from the principal investigator. However, the IRB may determine that a study shall require enhanced monitoring from sources (to be defined by the IRB) other than the investigator [45 CFR 46.103(b)(4), 21 CFR 56.108(a)].

Criteria that the IRB may use as a basis for requiring enhanced monitoring may include but are not limited to:
1) Randomly selected studies
2) Complex studies involving unusual levels or types of risks to subject
3) Studies conducted by investigators who previously failed to comply with applicable regulations or institutional or IRB requirements
4) Studies where other concerns have been raised by subjects, a DSMB, study or HSRO staff, IRB members or others about possible material changes occurring without IRB approval.
7.6 **NOTIFICATION LETTERS AND APPROVAL STAMPS**

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** February 25, 2009  
**Revised:** May 24, 2011

The HSRO shall notify Principal Investigators and institution leaders (when appropriate) in writing of IRB determinations relative to approval, disapproval, required modifications, suspensions, terminations and other information and matters for which such disclosure is required. Determination letters from the HSRO shall reference or describe the UM IRB number of the study, Principal Investigator, project title, date of the IRB action, the IRB action itself, and other pertinent information. Since the determination letters are generated electronically, language defining the electronic signature shall attest to the fact that these letters were prepared according to IRB and HSRO specifications. Such electronically-generated determination letters are considered by the IRB to be a sufficient statement of approval, disapproval or other IRB decisions and shall serve as official notification documents to sponsors or others.

Letters documenting the approval of initial or continuing studies or study amendments, no matter whether approved by expedited review or by the convened IRB, shall specify conditions and terms of approval. They shall be forwarded to the Principal Investigator with approved consent forms and other documents that require marking by the HSRO with an approval watermark or stamp.

The UM IRB approval watermark/stamp indicates that the document has been reviewed and approved by the IRB and shows the date the approval was granted. The watermark/stamp shall only be applied to finalized documents and shall appear on each page of the consent form. Commonly, the approval watermark/stamp is used for the following types of documents which may only be used with a valid watermark/stamp:

1. Consent documents  
2. Consent form addenda  
3. Assent documents  
4. Information sheets associated with the consent process (as directed by the IRB)  
5. Advertising/subject recruitment materials reviewed and approved by the IRB
Letters of approval of initial or continuing studies shall include the following information/instructions when applicable:

1) The Principal Investigator is responsible for compliance with all applicable federal regulations and UM written policies and procedures
2) It is necessary to retain signed consents by all subjects unless a waiver is granted
3) Participants must sign a consent form that has been watermarked/stamped in a manner that indicates IRB approval. Only the currently-approved watermarked/stamped consent forms may be used
4) Any and all modifications (amendments) to the protocol and consent form must be submitted to and approved by the IRB before implementation.
5) Continuing and final reports are required.

Letters of IRB disapproval shall specify any necessary actions required for securing IRB approval, if applicable.

The IRB has authority to modify consent forms and protocols in a manner it deems necessary to secure IRB approval. If such modifications have been made by the IRB and IRB approval is given to the study based in part on these modifications, approval letters shall indicate that modifications have been made. Letters shall also state that the study must be carried out, and the consent forms must contain the modifications, as approved by the IRB. If the Principal Investigator implements the study following notification that the IRB has made modifications, this action shall confirm that the Principal Investigator accepts the IRB modifications and is obligated to carry them out. If the Principal Investigator finds one or more of the IRB's modifications to be unacceptable, he/she shall return the acceptance letter to the HSRO and he/she may appeal the decision to the convened IRB within 30 days. If the Principal Investigator returns the acceptance letter to the HSRO, he/she must not implement the study until such time as IRB approval is given in another letter to the Principal Investigator.
SECTION 8: DEFINITION OF IRB REVIEW TYPES
8.1 **Exempt Studies**

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** March 31, 2006  
**Revised:** August 17, 2011

A study may be ‘exempt’ from IRB requirements pursuant to 45 CFR 46 if it involves very little if any risk to human subjects and if it fits within an "exempt" category listed under 45 CFR 46.101(b)(1)-(6). The categories are:

**EXEMPT CATEGORY 1.** Research conducted in established or commonly accepted educational settings involving normal education practices, such as (i) regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods. Research conducted in established or commonly accepted educational settings involving normal education practices, such as (i) regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

[NOTE – This exemption likely excludes research involving deception or withholding of information from subjects.]

**EXEMPT CATEGORY 2.** Research that is limited to the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey or interview procedures, or observation of public behavior unless information obtained from these sources is recorded in such a manner that human subjects can be identified (directly or through identifiers linked to the subjects), and any disclosure of the subject's responses outside the research could reasonably place the subject at risk of criminal or civil liability or be damaging to his or her financial standing, employability, or reputation.

[NOTE – This exemption does not apply to research involving children except for research involving educational tests or observation of public behavior where the investigators do not participate in the activities being observed, or interact directly with the children.]

**EXEMPT CATEGORY 3.** Research involving the use of education tests (cognitive, diagnostic, aptitude, achievement), survey or interview procedures, or observation of public behavior that is not exempt under exemption category (2) (above) if: (i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statutes require, without exception, that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
EXEMPT CATEGORY 4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

[NOTE – This exemption requires that the research material be existent (i.e. on the shelf) at the time the protocol is submitted to the IRB. The use of research material collected after the research is initiated will disqualify the study from exempt status.]

EXEMPT CATEGORY 5. Research and demonstration projects which are conducted by or subject to approval of [federal] 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 these programs; (iii) possible changes or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payments for benefits or services under those programs.

EXEMPT CATEGORY 6. Taste and food quality evaluations and consumer acceptance studies, (i) if wholesome food without additives is 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 by the Food and Drug Administration (FDA) or approved by the Environmental Protection Agency (EPA) or the Food Safety and Inspection Service of the U.S. Department Agriculture (USDA)

[NOTE – This exemption does not apply to studies involving alcohol, vitamins or food supplements.]
8.2 EXPEDITED REVIEWS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 31, 2006
Revised: August 17, 2011

8.2(A) GENERAL PRINCIPLES OF EXPEDITED REVIEWS

Approval of new or continuing studies may be made on an expedited basis by the IRB chair or designee of the IRB Chair. It is the responsibility of the IRB Chair to ensure that the designee has the required expertise and knowledge of IRB policies and procedures. Criteria for approval by expedited review are the same as those of the convened IRB (c.f. Policy 7.3) and the expedited review should be as meaningful and significant as that of the convened IRB (c.f. Sections 9 & Section 10).

A study may be forwarded by the HSRO for expedited review and approval if it is considered that the study involves no more than minimal risk to human subjects and if it fits under one or more of the nine categories qualifying a study for expedited review in accordance with federal regulations 45 CFR 46.110 and 21 CFR 56.110.

[NOTE – "Minimal risk" is defined by the OHRP and FDA 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 the daily life or during performance of routine physical or psychological examinations or tests."]

The expedited review category will not be used if identification of subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. The expedited review category shall also not apply to studies involving the use of investigational drugs, devices, or biologics for which an IND/IDE is required.

If the study qualifies for expedited review, the IRB chair or designee may approve the study, seek additional information from the principal investigator, require modifications to the study to gain approval or defer the study to the convened IRB. If the IRB chair or designee determines that the study does not qualify for expedited review, the IRB chair designee shall refer the study to the convened IRB. The IRB Chair or designee conducting an expedited review may not disapprove a study but rather must forward the study for review by the convened IRB if he/she believes disapproval is warranted.

A report of all studies approved under expedited criteria shall be forwarded to each IRB for its review on a monthly basis. If the convened IRB expresses concerns about an expedited study which, in its estimation, should not have been expedited, the study will be prepared for review by the convened IRB at a subsequent meeting.
8.2(B) CATEGORIES OF STUDIES QUALIFYING FOR EXPEDITED REVIEW

Studies may qualify for expedited review only if they fit within one or more of the following categories:

EXPEDITED CATEGORY 1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met:
   a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required; OR
   b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling

[NOTE – Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.]

EXPEDITED CATEGORY 2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
   a) From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; OR
   b) From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

EXPEDITED CATEGORY 3. Prospective collection of biological specimens or other biological information for research purposes by noninvasive means. Examples include but are not limited to:
   a) Hair and nail clippings in a nondisfiguring manner
   b) Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction
   c) Permanent teeth if routine patient care indicates a need for extraction
   d) Excreta and external secretions (including sweat)
   e) Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue
   f) Placenta removed at delivery
   g) Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor
   h) Supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques
   i) Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings
   j) Sputum collected after saline mist nebulization.
   k) Vaginal swabs that do not go beyond the cervical os
   l) Rectal swabs that do not go beyond the rectum
   m) Nasal swabs that do not go beyond the nares
EXPEDITED CATEGORY 4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) 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 subjects or an invasion of the subjects’s privacy
   b) Weighing or testing sensory acuity
   c) Magnetic resonance imaging
   d) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electoretinography, 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

EXPEDITED CATEGORY 5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

NOTE: This category includes research involving materials that were previously collected (retrospective/existing) for either non-research or research purposes, provided that any materials collected for research were not collected for the currently proposed research.

NOTE: This category permits research on materials collected prospectively but only if such materials are collected solely for non-research purposes.

EXPEDITED CATEGORY 6. Collection of data from voice, video, digital, or image recordings made for research purposes.

EXPEDITED CATEGORY 7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

The following two expedited review categories (8 & 9) pertain to continuing reviews but not to initial reviews
EXPEDITED CATEGORY 8. Continuing review of research previously approved by the convened IRB as follows:
   a) Where
      i. The research is permanently closed to the enrollment of new subjects
      ii. All subjects have completed all research-related interventions; AND
      iii. The research remains active only for long-term follow-up of subjects; OR
   b) Where no subjects have been enrolled and no additional risks have been identified; OR
   c) Where the remaining research activities are limited to data analysis.

[NOTE – For a multi-center study, an expedited review procedure may be used by the UM IRB whenever any of the above conditions are satisfied at the University of Miami site.]

EXPEDITED CATEGORY 9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.
8.3 REVIEWS REQUIRING THE CONVENED IRB

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 31, 2006
Revised: August 17, 2011

The HSRO and/or the IRB Chair and/or IRB-designee and/or the convened IRB shall recommend convened IRB review if a new or continuing study does not meet the criteria for exemption or for expedited review or if it is otherwise determined that the study requires review at a convened IRB meeting.

If a study is forwarded to the convened IRB for review, the IRB is responsible to make final decisions on the review category and may decide that the research may qualify for exemption or expedited review. If a study is recommended for convened IRB review, HSRO staff shall assign the specific IRB for this responsibility and shall assign primary and secondary reviewers with advice of the IRB chair or designee.
8.4 MULT-YEAR IRB APPROVAL

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: April 4, 2008
Revised: August 17, 2011

Note – this policy is approved under the UM IP^3R Program

8.4(A) GENERAL PRINCIPLES FOR MULTI-YEAR APPROVAL
At initial submission ('new studies') or at the time of continuing review ('on-going studies'), eligible studies may receive a three year approval (including the year of initial or continuing approval). If the study is undergoing expedited review, the reviewer (the IRB Chair or designee) may recommend such multiyear approval to the convened IRB for its approval. If the study is not undergoing expedited review but instead is being reviewed by the convened IRB, that panel may grant the three-year approval at its discretion.

To be eligible for the three year approval, the study must fit the criteria of the IP^3R Program (c.f. Section 2.5 of these Policies). Some (but not all) of these criteria include that the study or associated training:

a. is not federally funded and/or subject to federal, state or local regulations that require continuing review at least annually
b. does not involve drugs, devices or biologics for which an IND/IDE is required and/or is not subject to FDA regulations requiring continuing review at least annually
c. poses no more than minimal risk as determined by the IRB and is approved for no less than one year via the standard IRB approval process

8.4(B) PROCESS FOR GRANTING MULTI-YEAR APPROVAL
The process for granting multi-year approval shall occur as follows:

1. the expediting reviewers, or the convened IRB, shall notify the HSRO of the standard (i.e. up to one year) approval of the new or continuing study and the HSRO shall notify the principal investigator of this approval. This notification to the principal investigator shall occur so that the study may proceed in a timely manner without waiting for any subsequent deliberations as to whether the study shall receive multi-year approval
2. if an expediting reviewer (or a reviewing member of the convened IRB) believes that the study should be given three-year approval, he/she may so recommend to the convened IRB
3. by majority vote, the convened IRB may grant three-year approval to eligible studies upon recommendation of the expediting reviewer or a reviewing IRB member.

If three-year approval is granted by the IRB, the IRB shall notify the HSRO and the HSRO shall notify the principal investigator that the requirement for continuing review is waived for the approved duration.
The HSRO shall also notify the principal investigator of the conditional properties of this three-year approval (see below).

8.4(c) **CONDITIONS FOR CONTINUANCE OF MULTIYEAR STUDY APPROVAL**

During a three-year approval period, the study must remain unchanged from that reviewed and approved by the IRB with the exception of amendments approved in accordance with Section 11 of these IRB policies. For any amendment proposed during a three-year approval period, however, the convened IRB (or the Chair or designee in the case of expedited review) shall determine whether the amendment makes changes that are compatible or incompatible with three-year approval of the study and whether such three-year approval should therefore be continued.

If an amendment is determined to be compatible with the three-year approval status of the study, that status may continue. If an amendment is determined by the IRB (or expediting reviewer) to be incompatible with the three-year approval status of the study, the study status shall revert to requiring continuing review at least annually. If this occurs, the IRB (or the expediting reviewer) shall determine the date of expiration of its approval which shall be no later than one year after the approval date of the amendment.

As for all studies, the Principal Investigator of any study that receives three-year approval is responsible for reporting to the HSRO any deviation from the approved protocol, any serious study-related adverse events or unanticipated problem involving risk to subjects or others that might occur. The IRB has the authority to revert the study status to require continuing review at least annually. In the event of a serious study-related adverse event, the study status shall revert to requiring continuing review at least annually. If the study status does revert to require annual review, the IRB shall determine the date of expiration of its approval which shall be no later than one year from the date of the serious adverse event or the date that the IRB changes the study status.

8.4(d) **PRINCIPAL INVESTIGATOR AFFIRMATION**

At least annually, the principal investigator must affirm via ePROST to the HSRO that:

- a. the study protocol is unchanged from that granted multi-year approval by the IRB
- b. the risk to subjects is unchanged
- c. no study-related, serious adverse events occurred

As for other studies requiring continuing review, notices shall be forwarded to the Principal Investigator from the HSRO warning that this Principal Investigator Affirmation is due. If the affirmation is not received prior to or on the day at which IRB approval would have expired had the study not been given three-year approval, the study shall be suspended for expiration of IRB approval.

8.4(E) **CONTINUING REVIEW**

Studies granted three-year approval must receive continuing review at least once during every three years. As for other studies requiring continuing review, notices shall be forwarded to the Principal Investigator from the HSRO 90-, 60-, and 30-days prior to the day at which the three-year IRB approval
will expire warning that a continuing report is due. The continuing report may be approved (if appropriate) by an expedited reviewer. This approval shall be for up to one year so that the study may proceed in a timely manner without waiting for any subsequent deliberations as to whether the study shall retain multi-year approval. The convened IRB may again permit 3-year approval upon recommendation of the expediting reviewer per IP3R policy. If the continuing report is not undergoing expedited review but instead is being reviewed by the convened IRB, that panel may grant the three-year approval at its discretion.
SECTION 9: IRB REVIEW OF INITIAL STUDIES
9.1 INITIAL STUDIES – EXEMPT

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 31, 2006
Revised: August 18, 2011

The IRB Chair or designee shall make the final determination whether an initial study qualifies for exempt status by virtue of the fact that it provides no more than minimal risk and that it falls within the criteria required to be exempted from federal regulations. This decision shall be made according to regulations included in 45 CFR 46.101(b)(1)-(6), 21 CFR 56.104(d) and according to the UM policy defining these criteria (c.f. Policy 8.1). The IRB may grant exempt status only if all research activities within the study involve procedures listed under 45 CFR 46.101(b) and 21 CFR 56.104(d). The IRB shall not grant exempt status to research involving prisoners, human in vitro fertilization and to FDA-regulated research under categories 1-5 of 45 CFR 46.101(b). Research involving minors will be exempt on a limited basis under 45 CFR 46.101(b).

IRB Chairs or designees may use their discretion as to whether a study should be exempt or requires IRB review even if the study fulfills the criteria for exemption according to the regulations. The Chair or designee shall conduct a substantive and meaningful review of all materials related to the assigned study, conduct informal queries of the Principal Investigator and/or other experts as necessary to provide a thorough review and present clear and concise requirements/recommendations for changes and/or questions in written form (via ePROST, by email or otherwise) for communication to the Principal Investigator. The Chair or designee may request minor revisions and/or clarifications before approval for exemption is granted. The Chair or designee may request a second reviewer and/or may seek recommendations from an expert consultant(s) for issues which require expertise beyond, or in addition to, that available on the IRB.

If approved, the IRB Chair or designee shall document the exempt category that applies to the study. Policy 8.1 lists the exempt categories that are defined in federal regulations. 45 CFR 46 Part D and 21 CFR 50 Part D must be satisfied if the research involves minors and 45 CFR 46 Part B must be satisfied if the research involves pregnant women, fetuses, neonates of uncertain viability, placenta, dead fetuses or fetal material. This documentation shall be provided to the HSRO which is responsible for record-keeping and for creating correspondence to the Principal Investigator.

Approval of a study as exempt does not automatically include exemption from the informed consent or HIPAA authorization requirements. If exemptions from these requirements are requested by the Principal Investigator, these requests must be reviewed and decided upon by the IRB Chair or designee. If informed consent is required, the documents should contain all required elements unless an alteration is justified in writing by the Principal Investigator and approved by the IRB Chair or designee.
Regulations do not require continuing review of exempt research. However, the IRB chair or designee may require such reviews at his/her discretion.

The convened IRB shall be notified of exempt approvals in a timely manner. If the IRB Chair or designee does not approve a study as exempt, the chair or designee shall defer the study to expedited or convened IRB review by notifying the HSRO of this decision. The Principal Investigator shall be informed of this decision and its reasons. If the study is deferred for expedited review, the Principal Investigator may appeal this decision to the IRB chair. If the study is deferred for review by the convened IRB, the Principal Investigator may appeal this decision to the convened IRB.

All changes in exempt studies must be reported to the IRB for review and approval prior to implementation. The IRB and Principal Investigators shall understand that the criteria to exempt a study from federal regulations must remain applicable during the entire time that an exempt study remains active and that certain changes may disqualify the research from exempt status.
9.2 INITIAL STUDIES – EXPEDITED

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** March 31, 2006

The IRB Chair or the Chair’s designee from among the IRB members shall determine whether a study involves no more than minimal risk and may be reviewed and approved within the "expedited category". This decision shall be made according to regulations included in 45 CFR 46.110, 45 CFR 46.111, 21 CFR 56.110, 21 CFR 56.111, and 38 CFR 16.110. 38 CFR 16.111) and according to the UM policy defining these criteria *(c.f. Policy 8.2)*

[**NOTE** – See also [http://www.hhs.gov/ohrp](http://www.hhs.gov/ohrp)]

If the IRB Chair or designee disagrees with the applicability of expedited review for a given study, the Chair or designee may refer the study to the convened IRB by notifying the HSRO of this decision. Even if the submission fulfills the criteria for expedited review according to the regulations, the Chair or designee may use his/her discretion as to whether the study should be expedited or referred for convened IRB review.

In conducting an expedited review of an initial study, the IRB Chair or designee may exercise all of the authorities of the IRB with the exception of disapproval of the study. The Chair or designee shall conduct a full, significant and meaningful review of all materials related to the assigned study, inquire of the Principal Investigator and/or other experts as deemed necessary and present clear and concise requirements/recommendations for changes and/or questions in written form (via ePROST) for communication to the Principal Investigator. The Chair or designee may request minor revisions and/or clarifications from the Principal Investigator before approval is granted. The chair or designee may request a second reviewer and/or may seek recommendations from an expert consultant(s) for issues which require expertise beyond, or in addition to, that available on the IRB.

Approval by the IRB chair or IRB-designee of a study under the expedited review process requires:

a) Confirmation that the research poses no more than minimal risk  
b) Identification of the specific permissible category of expedited review into which the study falls  
c) Determination of the requirement for continuing review and additional requirements  
d) Review of the informed consent process in accordance with regulations  
e) Review of any recruitment procedures involving advertisements  
f) Documentation of the above findings
Written Policies and Procedures for the Protection of Human Subjects in Research

Written Policies and Procedures for the Protection of Human Subjects in Research

If the chair or IRB-designee approves the study on an expedited basis, he/she shall determine the interval to a required continuing review. This interval shall not be greater than one year from the date of the initial IRB approval.

If expedited approval is granted by the IRB Chair or designee, he/she shall:

a) Document the expedited category(ies) that applies to the study

[NOTE – A children’s category (under 45 CFR 46 SubPart D and/or 21 CFR 50 SubPart D) must be identified if any minors under the age of 18 years are involved as research participants, and 45 CFR 46 SubPart B must be satisfied if the research involves pregnant women, fetuses, neonates of uncertain viability, placenta, dead fetus, or fetal material. New Studies involving 45 CFR 46 SubPart C (i.e. research involving prisoners) shall not be reviewed in an expedited manner.]

b) Comment on the review of informed consent (unless a waiver of consent was approved)

c) Provide required findings if a waiver of consent or alteration of consent (45 CFR 46.116(c) or (d)) or waiver of documentation of informed consent (45 CFR 46.117(c)(1 or 2) is requested/approved.

This documentation shall also include approval period dates (if less than annual continuing review is recommendation) and detail limitations to approval periods (such as limitations to enrollment numbers prior to reporting back for continuing review.

The IRB Chair or IRB-designee shall provide the documentation (above) to the HSRO which is responsible for record-keeping and for creating correspondence to the Principal Investigator. The HSRO shall ensure that notification of expedited review approval is made at the next convened IRB meeting.

If the IRB Chair or designee is not able to approve the study, the Principal Investigator shall be informed of the reasons and may request convened IRB review.

Throughout these studies, the requirements for informed consent (or its waiver or alteration) apply to all studies meeting criteria for approval on an expedited basis.
9.3 INITIAL STUDIES – CONVENED IRB REVIEW

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: July 24, 2006
Revised: August 18, 2011

Studies being reviewed by the convened IRB shall be assigned at least one primary and one secondary reviewer. Primary reviewers shall be prepared to lead the discussion of the study, the complete grant application (as applicable), all other materials related to the study and the risk/benefit ratio. Primary reviewers are encouraged to seek expertise/consultation as necessary, to conduct informal queries of the Principal Investigator and other experts in order to provide a thorough review, and to coordinate review comments/questions with the secondary reviewer(s) if appropriate. Primary reviewers shall present specific recommendations for IRB actions, including changes and/or questions for the Principal Investigator.

Secondary reviewers shall be prepared to serve in the absence of the primary reviewer. Secondary reviewers are also encouraged to seek expertise/consultation as necessary, to conduct informal queries of the Principal Investigator and other experts in order to provide a thorough review and to coordinate review comments/questions with the primary reviewer(s) if appropriate. Secondary reviewers may present specific recommendations for IRB actions, including changes and/or questions for the Principal Investigator.

IRB members shall receive all appropriate study materials with sufficient time for their review prior to scheduled IRB meetings to be prepared to participate in deliberations and voting. After presentation by the primary and/or secondary reviewers and deliberations at IRB meetings, any IRB member may motion for an action. For a motion to pass, the majority of voting members present must vote affirmatively. The convened IRB may approve motions and thereby take any of the actions indicated below:

1) **APPROVED AS SUBMITTED**
   This motion defines the study as approved as submitted, with no further action required. In this case, the HSRO shall inform the Principal Investigator in writing of the approval and its duration. The start date for the study shall be the date of this IRB approval, and the study may begin upon receipt of the letter of approval.

2) **APPROVED AS MODIFIED BY THE IRB**
   This motion defines the study as approved with revisions, clarifications or other changes to the protocol or to the informed consent or other documents made by the IRB. In this case, the HSRO shall inform the Principal Investigator in writing of the changes made by the IRB and of
the IRB approval of the study including those changes and also including the duration of approval.
The letter to the Principal Investigator from the HSRO shall state that the Principal Investigator must conduct the study as modified by the IRB in accordance with the IRB approval.

If the Principal Investigator does not accept the changes made by the IRB, he/she may not initiate the study pursuant to the IRB approval and that IRB approval is to be considered void. The study may not be started unless/until a new IRB approval is obtained and confirmed in writing to the Principal Investigator by the HSRO.

If the Principal Investigator does not accept the changes made by the IRB, he/she may withdraw the study, appeal to the IRB or make revisions to the study for reevaluation by the IRB.

3) **DEFERRED FOR SUBSEQUENT EXPEDITED REVIEW BY THE IRB CHAIR OR DESIGNEE**

This motion defines that the IRB has agreed to approve the study but with conditions that require revisions and/or clarifications that the IRB determined to be nonsubstantive and minor and not directly relevant to the IRB determinations required under 45 CFR 46.111 and/or 21 CFR 56.111. Such revisions or clarifications may be reviewed and approved by the IRB chair or designee on an expedited basis.

Required revisions or clarifications must be submitted to the HSRO by the Principal Investigator within 30 calendar days following notification to the Principal Investigator by the HSRO unless the IRB requires a due date that is different from that occurring 30 days following notification.

Pursuant to this motion, the HSRO shall notify the Principal Investigator that the revisions and/or clarifications shall be reviewed on an expedited basis by the IRB Chair or designee. The IRB shall clearly specify the action(s) needed and who has the authority to review and approve the revised or requested materials on an expedited basis. A letter shall be forwarded to the Principal Investigator by the HSRO indicating the specific required action(s) and the fact that the documents may be returned for review on an expedited basis and that another convened IRB review may not be required unless the study is deferred to the convened IRB by the IRB Chair or designee. The letter shall also define that the study has been deferred and has not received IRB approval and that the study must not be initiated until the IRB Chair or designee has approved it on behalf of the IRB.

If the study is subsequently approved by the IRB Chair or designee, the HSRO shall inform the Principal Investigator of this approval and that the date of approval is the date that the fully-convened IRB deferred the study and set conditions for its expedited re-review rather than the date that the minor changes were approved on an expedited basis by the IRB Chair or IRB-designee. The study may begin upon receipt of this letter of approval.
If revisions and/or clarifications are submitted after the due date, the Chair/designee may seek an explanation from the Principal Investigator and/or:
   a. Defer the study to the convened IRB for its review and approval/disapproval; **OR**
   b. Defer the study to the IRB for withdrawal. If the IRB withdraws the study, the Principal Investigator may re-submit a new application for the study incorporating the revisions and/or clarifications from the prior IRB review; **OR**
   c. Find the explanation and the revisions and/or clarifications acceptable and approve the study

4) **DEFERRED FOR SUBSEQUENT RE-REVIEW BY THE CONVENED IRB**
   This motion defines the study as needing revisions or clarifications from the Principal Investigator for subsequent review by the convened IRB. This motion shall pertain when the convened IRB has determined that the revisions or clarifications are substantive and directly relevant to the IRB determinations required under 45 CFR 46.111 and/or 21 CFR 56.111. In this case, the Principal Investigator shall be informed by the HSRO in writing of the needed revisions and/or clarifications and the requirement that these revisions or clarifications be submitted within 30 calendar days unless otherwise specified by the IRB. The letter shall make clear that the study is not approved and the revisions and/or clarifications will be reviewed at a convened IRB meeting.

   If the study is subsequently approved by the convened IRB, the HSRO shall inform the Principal Investigator of this approval and that the date of approval is the date that the fully-convened IRB gave final approval to the study. The study may begin upon receipt of this letter of approval.

   If revisions and/or clarifications are submitted after the due date, the HSRO shall seek an explanation from the Principal Investigator and the IRB may either conduct its review or it may withdraw the study. If the IRB withdraws the study, the Principal Investigator may re-submit a new application for the study incorporating the revisions and/or clarifications from the prior IRB review.

5) **TABLED**
   This motion defines the situation if the IRB is unable or unwilling to review and/or vote on a study or other matter. This may occur if the quorum is lost, pertinent documents are unavailable or the scope of IRB expertise is not considered sufficient for appropriate decision-making. Although the Principal Investigator may be notified of this motion, no action by the Principal Investigator is required.
6) **DISAPPROVED**

This motion defines the study as not approved by the IRB for reasons directly relevant to the IRB determinations required under 45 CFR 46.111 and/or 21 CFR 56.111 such as that the study requires major changes or that it is not likely to be feasible without a complete reassessment of the protocol by the Principal Investigator and/or sponsor. In this case, the HSRO shall inform the Principal Investigator in writing of the disapproval. The letter shall include a description of the reasons why the IRB has taken this action and shall inform that the Principal Investigator has an opportunity to respond to the IRB in person or in writing. If the Principal Investigator appeals the disapproval, it is the responsibility of the IRB to ensure that there is a fair hearing of the appeal.
SECTION: 10 IRB REVIEW OF CONTINUING STUDIES
10.1 GENERAL PRINCIPLES FOR REVIEW OF CONTINUING STUDIES

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: April 24, 2006
Revised: August 18, 2011

Consistent with federal regulations, it is the policy of the University of Miami IRB that all human subject research activities (with the exception of 'exempt' studies and studies given multi-year approval by the IRB under IP3R policies) under its jurisdiction be reviewed at least annually with the period appropriate to the degree of risk [45 CFR 46.109(e), 21 CFR 56.109(f)]. This continuing review is additional to the review required for all changes, amendments, serious adverse events and sponsor notifications.

The IRB must determine at the time of initial approval and also at the time of each continuing report whether future continuing reports are to be submitted on an annual basis or whether it is necessary for continuing reports to be submitted more frequently [45 CFR 46.103(b)(4), 21 CFR 56.108(a)]. This is based on whether the risks are of a sufficient magnitude that annual review is inadequate. Although the magnitude of the risks is in part determined by the study procedures, other factors that pertain to the study (e.g., age of participants) may also be considered.

Regulations make no provision for any grace period extending the conduct of research beyond the date that IRB approval expires. Regulations also make no provision for retroactive approval of studies that have expired. Therefore, Principal Investigators have the responsibility to avoid lapses in IRB approval by submitting applications for continuing review and re-approval of a study with sufficient time for review prior to the previously assigned IRB expiration date. If IRB approval is not granted by the expiration date, the research is automatically suspended. Suspension for lapse in IRB approval means that new subjects can no longer be enrolled (see below) and research may not be conducted unless/until approval is granted.

If a study is suspended for lapse in IRB approval, the HSRO shall inform the Principal Investigator of this suspension and of related policies. Included in this policy information shall be the following:

d) It is the responsibility of the Principal Investigator to immediately submit either a continuing report or a final report

e) If IRB approval for continuance of the study is not granted before the close of the 90th calendar day following the lapse in IRB approval, the study shall be administratively closed unless this closure is waived by the Associate Vice Provost for Human Subject Research.

f) If the Principal Investigator wishes to continue the study, the continuing report should be immediately submitted but in no case should it be received by the HSRO later than 45 calendar days following lapse in IRB approval. This provides the IRB with 45 days to conduct its review prior to the 90th day and administrative closure of the study.
Continuing reports and their reviews should be substantive and meaningful with concentration upon the summary of the current state of the research, (number of subjects enrolled, number of subjects withdrawn and the reasons why, amendments, etc.), including whether the risk/benefit ratio has changed, whether there are unanticipated findings involving risks to human subjects and/or others, and whether any new information regarding risks and benefits should be provided to subjects and other information the institution and/or IRB deems necessary to conduct a meaningful review. An application to continue an active study shall be reviewed based on approval criteria that are the same as for initial (i.e. new) studies (c.f. Policy 7.3).

If the IRB is conducting continuing review in multi-center trials monitored by a DSMB, DMC, or other similar body or sponsor where relevant data/information may not be readily available to local investigators, the IRB may request/require and rely upon a current statement from the DSMB or sponsor indicating that it has reviewed study-wide adverse events, interim findings, and any recent literature that may be relevant to the research (in lieu of requiring that this information be submitted directly to the IRB and in addition to reports of local, on-site events and unanticipated problems).
10.2 CONTINUING STUDIES – EXPEDITED

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 31, 2006
Review: August 18, 2011

Those studies recommended for review under the expedited criteria are made available to the IRB Chair or designee of the Chair who shall be a member of the IRB. IRB Chairs and designees shall conduct reviews of studies that fit within the expedited criteria on behalf of the IRB. IRB chairs/IRB-designees may determine that studies recommended for expedited review require "Convened Board Review". The IRB may determine that studies recommended for Convened Board Review require exempt or expedited review.

Investigators are urged to consult with HSRO regulatory staff before making their recommendations to the HSRO and the IRB regarding the review category.

Studies initially approved via expedited review are eligible for expedited review at the time of their IRB-defined continuing review; if, during the course of the study, the risks of these studies has not increased and the investigator is not proposing changes that affect the "minimal risk" designation. Such changes, or other information presented during an approved period or with the submission of a continuing review application, may impact the review category and disqualify the study from being approved on an expedited basis. In this case, the IRB Chair or designee shall determine the appropriate review category and the study may be forwarded to the convened IRB for full review.

Even if the submission fulfills the criteria for expedited review according to the regulations, the Chair or designee shall use his/her discretion as to whether the study should be expedited or referred for convened IRB review. The Chair or designee shall review all materials related to the assigned study, conduct informal queries of the Principal Investigator and/or other experts as necessary to provide a thorough review and present clear and concise requirements/recommendations for changes and/or questions in written form (by ePROST, email or otherwise) for communication to the Principal Investigator. The Chair or designee may request minor revisions and/or clarifications before approval is granted. The Chair or designee may request a second reviewer and/or may seek recommendations from an expert consultant(s) for issues which require expertise beyond, or in addition to, that available on the IRB.

If previously met criteria for expedited review have not changed since the most recent IRB review and approval, continuing review may be conducted under the same expedited review category(ies). Studies that were previously reviewed by the convened IRB may receive expedited review if the IRB has documented its decision that the study involves "minimal risk" and is eligible for future expedited review or if the IRB Chair or designee concludes that the study meets the following criteria:
Option 1:
1) The research is permanently closed to the enrollment of new participants; AND
2) All enrolled participants have completed all study-related procedures and interventions; AND
3) The research remains active only for long-term follow-up of participants.

Option 2:
No participants have ever been enrolled at this site and no additional risks have been identified.

Option 3:
The remaining research activities are limited to data analysis.

Notification of approvals of expedited continuing reviews shall be made in a timely manner to the convened IRB. If the Chair/designee cannot approve a continuing study, the review shall be deferred to the convened IRB and the Principal Investigator shall be informed of the reasons and may provide additional or clarifying information to the convened IRB.
10.3 CONTINUING STUDIES – CONVENED IRB REVIEW

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: July 24, 2006
Revised: August 18, 2011

All appropriate materials from those studies recommended for continuing review under the "Convened Board Review" category shall be made available to all members of the convened IRB prior to scheduled IRB meetings. After presentation by the primary and/or secondary reviewers and deliberations at IRB meetings, any IRB member may motion for an action. For a motion to pass, the majority of voting members present must vote affirmatively. The convened IRB may approve motions and thereby take any of the actions relative to continuing studies indicated below:

1) APPROVED AS SUBMITTED
   This motion defines the study as approved as submitted, with no further action requested or required. In this case, the HSRO shall inform the Principal Investigator in writing of the approval and its duration. The Principal Investigator shall be informed by the HSRO in writing of the IRB approval and its duration.

2) APPROVED AS MODIFIED BY THE IRB
   This motion defines the continuing study as approved with revisions, clarifications or other changes to the protocol or to the informed consent or other documents made by the IRB. In this case, the HSRO shall inform the Principal Investigator in writing of the changes made by the IRB and of the IRB approval of the study including those changes and also including the duration of approval.

   The letter to the Principal Investigator from the HSRO shall state that the Principal Investigator must conduct the study as modified by the IRB in accordance with the IRB approval. If the Principal Investigator does not accept the changes made by the IRB, he/she:

   a) May withdraw the study, appeal to the IRB or make revisions to the study for reevaluation by the IRB; AND

   b) May not continue the study beyond the previous approval period. In this circumstance, the study shall be suspended on the day that the previous IRB approval has expired.

3) DEFERRED FOR SUBSEQUENT EXPEDITED REVIEW BY THE IRB CHAIR OR DESIGNEE
   This motion defines that the IRB has agreed to approve the continuing study but with conditions that require revisions and/or clarifications that the IRB determined to be nonsubstantive and minor and not directly relevant to the IRB determinations required under 45 CFR 46.111 and/or 21 CFR 56.111. Such revisions or clarifications may be reviewed and approved by the IRB Chair or designee on an expedited basis.
Required revisions or clarifications must be submitted to the HSRO by the Principal Investigator within 30 calendar days following notification to the Principal Investigator by the HSRO unless the IRB requires a due date that is different from that occurring 30 days following notification.

Pursuant to this motion, the HSRO shall notify the Principal Investigator that the revisions and/or clarifications shall be reviewed on an expedited basis by the IRB chair or designee. The IRB shall clearly specify the action(s) needed and who has the authority to review and approve the revised or requested materials on an expedited basis. A letter shall be forwarded to the Principal Investigator by the HSRO indicating the specific required action(s) and the fact that the documents may be returned for review on an expedited basis and that another convened IRB review may not be required unless the study is deferred to the convened IRB by the IRB Chair or designee. The letter shall also define that the study has been deferred and that the continuing report has not received IRB approval and that, if approval is not given prior to the date that prior IRB approval lapses, the study must be suspended on that expiration date. The study may not be continued beyond the expiration date of the prior approval and the suspension of the study will continue until the continuing report is approved.

Continuing Review of a study that is deferred for subsequent expedited review by the IRB Chair or designee must occur within one year of the date that the fully-convened IRB deferred the study and set conditions for its expedited re-review rather than the date that the minor changes were approved on an expedited basis by the IRB Chair or IRB-designee.

If revisions and/or clarifications are submitted after the due date, the Chair/designee may seek an explanation from the Principal Investigator and/or:

a) Defer the study to the convened IRB for its review and approval/disapproval; OR

b) Defer the study to the IRB for withdrawal. If the IRB withdraws the study the Principal Investigator may re-submit a new application for the study incorporating the revisions and/or clarifications from the prior IRB review; OR

c) Find the explanation and the revisions and/or clarifications acceptable and approve the study for continuation.
4) **DEFERRED FOR SUBSEQUENT RE-REVIEW BY THE IRB**

This motion defines that the study proposed for continuation needs revisions or clarifications from the Principal Investigator for subsequent approval by the convened IRB. This motion shall pertain when the convened IRB has determined that the revisions or clarifications are substantive and directly relevant to the IRB determinations required under 45 CFR 46.111 and/or 21 CFR 56.111. In this case, the Principal Investigator shall be informed by the HSRO in writing of the needed revisions and/or clarifications and the requirement that these revisions or clarifications be submitted within 30 days calendar days unless otherwise specified by the IRB. The letter should make clear that the continuing study is not approved and that it must be suspended on the date that prior approval expires unless it is subsequently approved for continuation prior to that expiration date. If a study that is deferred for subsequent re-review by the IRB is suspended because of a lapse in approval, this suspension will continue unless/until approval for continuation is approved by the convened IRB.

If the study is subsequently approved by the convened IRB, the HSRO shall inform the Principal Investigator of this approval and that the date of approval is the date that the fully-convened IRB gave final approval to the study.

If revisions and/or clarifications are submitted after the due date, the HSRO shall seek an explanation from the Principal Investigator and the IRB may either conduct its review or it may withdraw the study. If the IRB withdraws the study, the Principal Investigator may re-submit a new application for the study incorporating the revisions and/or clarifications from the prior IRB review.

5) **TABLED**

This motion defines the situation if the IRB is unable or unwilling to review and/or vote on a continuing study or other matter. This may occur if the quorum is lost, pertinent documents are unavailable or the scope of IRB expertise is not considered sufficient for appropriate decision-making. Although the Principal Investigator may be notified of this motion, no action by the Principal Investigator is required.

The fact that the review of a continuing study is tabled by the IRB does not change the expiration date of the prior approval or the consequences of a lapse in such approval.
6) **DISAPPROVED**

This motion defines the continuing study as not approved by the IRB for reasons directly relevant to the IRB determinations required under 45 CFR 46.111 and/or 21 CFR 56.111 such as that the study requires major changes or that current knowledge leads to the belief that it is not likely to be feasible without a complete reassessment of the protocol by the Principal Investigator and/or sponsor. In this case, the HSRO shall inform the Principal Investigator in writing of the disapproval. The letter shall include a description of the reasons why the IRB has taken this action and shall inform that the Principal Investigator has an opportunity to respond to the IRB in person or in writing with justification for a reversal of the decision or a proposal to change the protocol, which may be a basis for IRB reconsideration. If the Principal Investigator appeals the disapproval, it is the responsibility of the IRB Chair and members to ensure that there is a fair hearing of the appeal.

The fact that an appeal by the Principal Investigator is on-going does not change the expiration date of the prior approval or the consequences of a lapse in such approval.
SECTION 11: AMENDMENTS
11.1 **GENERAL PRINCIPLES**

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** February 21, 2006  
**Revised:** February 13, 2012

Prior to their implementation, all modifications to an ongoing study must be submitted to the HSRO and approved by the IRB pursuant to regulations and these policies. Examples of study modifications include those related to the protocol or informed consent documents or process, staffing, advertisements, number of subjects to be enrolled, questionnaires, etc.

The only case where a change can be made to an approved study without prior IRB approval is when the change is necessary to eliminate apparent immediate hazards to human subjects [45 CFR 46.103(b)(4)(iii), 21 CFR 56.108(a)(3) and (4)]. In this case, the Principal Investigator must notify the IRB of such changes in writing within ten (10) working days of the occurrence. This notification should be on the amendment forms supplied by the HSRO. To obtain IRB approval for study amendments, the Principal Investigator must submit to the HSRO an Amendment Form describing all proposed modifications. Upon receipt of this form, an HSRO staff member will recommend into which category the amendment fits (c.f. Section 11.2) and forward the amendment for further review pursuant to that category. Any significant new findings that arise from the review process and that might decrease participants’ willingness to continue participation must be provided to participants through re-consenting or other process as determined by the IRB. All members of the IRB will be informed of amendments that are approved using the expedited review process.

Amendments will only be approved for studies with active IRB approval. Approval of a study amendment shall not extend the length of study approval or the expiration date of that approval.

Upon final approval of amendments, modified consent/assent materials or recruitment/advertising materials will receive a stamp/watermark of approval and correspondence will be sent to the Principal investigator indicating what modified documents were approved.
11.2 TYPES OF AMENDMENTS AND THEIR REVIEW

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: February 21, 2006
Revised: February 13, 2012

The UM recognizes three categories of amendments which are:

1) **Informational Amendments:**
   These define changes that are informational or editorial without what reasonably may be considered potential risk implications for human subjects. Examples of informational amendments include (but are not limited to):
   - i. Addition of a study team member
   - ii. Replacement of a study team member into a position for which he/she is similarly qualified
   - iii. Changing a study title
   - iv. Changing a department affiliation or telephone number
   - v. Deleting items from a questionnaire without material change to the study
   - vi. Revision of the format of consent documents, recruitment materials or questionnaires
   - vii. Removal of a performance site

   The HSRO will pre-screen an amendment to determine whether it fits the informational category and, if it does, the HSRO will forward the amendment to an HSRO staff member who has been authorized by the IRB Chair as an administrative-designee. The administrative designees may request additional information from the Principal Investigator, approve the informational amendment or, if appropriate, he/she may defer a decision and refer the amendment to the IRB Chair or to an IRB member who is a Chair-designee or to the convened IRB. Such a deferral shall be made if, for example, the administrative-designee determines that the amendment does not meet the definition of “informational amendment.” The administrative-designee may not disapprove the amendment but, when he/she believes disapproval may be appropriate, shall recommend that the amendment be reviewed by the IRB Chair, IRB Chair-designee or convened IRB.
2) **Minor Procedural Amendments:**

These define minor changes that alter procedures but are reasonably considered to have no or minimal potential risk implications for human subjects. Examples of minor procedural amendments include (but are not limited to):

- Drawing slightly different amounts of blood
- Changing the frequency at which blood is drawn
- Adding to the number of planned research participants
- Revising the wording (but not the message) of the consent form
- Decreasing the drug dosage or frequency of drug administration
- Changing the recruitment plan
- Adding a standard quality-of-life questionnaire
- Initiating videotaping of subjects
- Adding non-sensitive questions to a questionnaire
- Changing the Co-Investigator (for minimal risk studies)
- Adding a performance site

Minor procedural amendments should be submitted to the HSRO where they will be pre-screened to confirm that they fit within this category. Such amendments will then be forwarded to the IRB Chair or IRB-designee for review. The IRB Chair or IRB-designee may request additional information from the Principal Investigator, approve the amendment on an expedited basis or, if appropriate, defer a decision and refer the amendment to the convened IRB.

Keys to determining the appropriateness of an expedited review of minor procedural amendments include that the revisions must:

- Not alter the risk/benefit ratio
- Not be significant in complexity or content to decrease a subject's willingness to participate or continue to participate
- Be no more than minimal risk

The IRB Chair or IRB-designee shall not disapprove the modification by expedited review but, when he/she believes disapproval may be appropriate, shall recommend that the revision be reviewed by the convened IRB.

3) **Risk-relevant Procedural Amendments:**

These define changes that may affect risk to human subjects in a manner that may not be considered as “minimal.” Such amendments often reflect changes in the direction of a study that may substantially change its purpose or goals. Examples of changes that shall be considered risk-relevant procedural amendments include (but are not limited to):

- Adding a new activity that may increase risk to participants
- Changing study drugs or medications
- Adding a vulnerable population
- Changing radiation exposure
v. Making changes to questionnaires or interviews that raise sensitive issues not previously raised
vi. Adding or changing invasive procedures
vii. Adding a research arm to the study
viii. Changing the Principal Investigator
ix. Changing the Co-Investigator (for studies with risk greater than minimal)

Risk-relevant Procedural Amendments should be forwarded to the HSRO where they will be pre-screened to determine if they may fit this category. Such amendments shall then be referred to the convened IRB for review and approval. In determining the level of risk to the amended study, the IRB may shorten the approval period. The IRB may also require a separate review, or a higher level of review of the study than was received on the original or most recent continuing review, as a result of the proposed amendment. The IRB may also require revisions to other application materials in relation to the proposed amendment.
11.3 CHANGING PRINCIPAL INVESTIGATORS

Requests to change the Principal Investigator (PI) of an active study must be forwarded within an Amendment Form for review on an expedited basis by the IRB chair or IRB-designee. If the Chair-designee believes that review by the convened IRB is required, the request shall be forwarded to the IRB for its review. Such request shall include a letter from the current PI indicating the change in responsibility and its rationale and a letter from the new PI accepting responsibility for the research. If the PI has left the University or is unable to provide an explanatory letter, the amendment/request to change the PI may come from the chair of the academic department or the director of the institutional research center that provides the administrative support and oversight to the study.

If the PI requesting the change within an active study holds an IND or IDE for the study, he/she must decide whether to continue to hold the IND/IDE or to transfer the IND/IDE to the new PI. In the latter case, the current PI (the IND/IDE holder) must inform the FDA in writing that he/she is turning over the IND number and responsibilities to the new PI; and the new PI must inform the FDA in writing of acceptance of the responsibility for the IND number and that all documents relating to the IND have been transferred to him/her.

Co-Investigators provide additional leadership to a study and may bring to the study similar or complementary expertise required for study conduct. Requests to change (or remove) a Co-Investigator may be reviewed and approved by an IRB Chair or-designee through the expedited process. The IRB Chair or designee will ensure that the change or removal of the Co-Investigator does not lead to increased risk to the subjects and is made in accordance with prior IRB determinations related to the study. If the Chair believes that review by the convened IRB is required, the request shall be forwarded to the IRB for its review.

Additionally, any absence by the PI expected to last 30 calendar days or more requires the submission of a notification to the IRB detailing how the study will be conducted during this absence and who will provide oversight of the study conduct during the PI's absence from the institution (i.e. leave, sabbatical, etc.).
11.4 INFORMATIONAL MATERIALS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: April 10, 2006
Revised: February 13, 2012

Informational materials such as Investigator's Brochures, updated package inserts and any other materials requiring submission via a Notification (reportable event) in ePROST should be submitted to the HSRO in a timely manner. The HSRO shall acknowledge receipt of such materials either by correspondence to the principal investigator or by executing the 'Acknowledged/Noted' activity in ePROST. The HSRO shall make these items available to the IRB Chair or designee who shall determine whether further IRB action is required. If no further IRB action is required, the material shall be added to the study file kept by the HSRO. If further action is required, the IRB Chair or designee may request that the HSRO seek information or modifications from the principal investigator or he/she may refer the submission to the convened IRB for its deliberation and resolution. Investigators are reminded that all changes in research, including changes to study personnel, must be submitted as an Amendment and not in a Notification form. Notification forms communicating changes in research shall not be accepted by the HSRO.
11.5 STUDY EXCEPTIONS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: April 4, 2006
Revised: February 13, 2012

As defined in policies on Amendments (c.f. Section 11), Principal Investigators are required to obtain IRB approval for changes in studies. Although such changes/amendments are usually permanent and affect all or most study participants, there may be occasions when the Principal Investigator wishes to make a temporary change in a protocol or a change that pertains only to one or a few participants. These temporary or limited changes are defined as "study exceptions".

Examples of "study exceptions" may include:
   a) Enrollment of a study participant who does not meet the eligibility criteria, such as whose age slightly exceeds the age criterion
   b) Changing the dose of a study medication
   c) Changing a visit date
   d) Adding an extra visit or omitting a visit

All study exceptions must receive IRB approval prior to initiation and must be listed in the ensuing continuing report. Submission and review of study exceptions shall follow the policies defined for submission and review of Amendments. Whether expedited review by the IRB Chair or designee or by the convened IRB, the review deliberation shall take into account all relevant materials as well as a determination as to whether the exception falls either within the specified guidelines of the approved protocol or is specifically approved by the sponsor. The review shall also be based on a determination as to whether the exception can affect the well-being of subjects (either favorably or adversely).

When submitting a request to the HSRO for IRB approval of a study exception, the Principal Investigator should include such information as:
   a) What are the limitations of the exception
   b) Why the exception is the best choice for the subject
   c) How the exception differs from the approved protocol
   d) Whether the trial sponsor (if any) approves the exception
   e) Whether the data collected as a result of the exception will be analyzed in a manner different from that of other data
   f) Whether the exception changes the risk/benefit
   g) Whether or not an amendment to the study is intended to follow
If an exception is required in an emergency for a life-threatening situation before IRB approval can be obtained, the Principal Investigator may implement the changes but must notify the IRB of such changes in writing within ten (10) working days of the occurrence. This notification must be submitted in the ePROST amendment form if the changes will apply to the entire study or via a Notification if the changes are limited to one or a few participants. In either case, the submission must explain why the exception was necessary to eliminate immediate hazards to human subjects [45 CFR 45.103(b)(4)(iii), 21 CFR 56.108(a)(3) and (4)].
SECTION 12: CLOSING STUDIES AND FINAL REPORTS
12.1 CLOSING STUDIES AND FINAL REPORTS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: October 16, 2006
Revised: February 13, 2012

Regulations (45 CFR 46.103/21 CFR 56.108) require prompt reporting to the IRB of changes in a research activity including study completion and closing.

Studies approved under exempt criteria do not require submission of a final report. Rather, Principal Investigators may close exempt studies by submitting an affirmation in writing to the HSRO that study activities are complete.

Principal Investigators may recommend closure of studies approved under expedited criteria or by the convened IRB if all of the following conditions are met:

1) All subject enrollment at UM-approved sites is complete; AND
2) All data (including study follow-up data) pertaining to human subjects have been collected; AND
3) No further human subject interaction is planned for the purpose of research; AND
4) No further analysis of identifiable private information or biological specimens is to be conducted.

Industry sponsored studies may be closed upon recommendation of the Principal Investigator if either of the following apply:

1) The University of Miami site is closed by the sponsor. In this case, the final report must include a notification (letter or email) from the sponsor or sponsor's representative indicating that the University of Miami site is closed and that individually identifiable data are no longer being collected on subjects at this site [NOTE - Data analysis may be ongoing by the sponsor at another site, but data analysis may not be ongoing by the UM Principal Investigator]; OR
2) The Principal Investigator has withdrawn his/her participation in the sponsor's protocol. In this case, the Principal Investigator must include a copy of the notification to the sponsor (letter or email) with the final report

To close a non-exempt study, the Principal Investigator must submit a final report specific to that study. If IRB approval of a study has lapsed prior to approval of a final report, the study shall be suspended and the final report must include a description of activities that have occurred in the study since approval of the prior continuing report.
Final reports may be reviewed and approved by an “expedited” process. This expedited review may be conducted by an IRB chair, an IRB-designee or an administrative-designee. In this circumstance, the reviewer may approve the final report and close the study or, if appropriate, he/she may defer a decision and refer the final report to the convened IRB.

Final reports may be reviewed and approved by an administrative-designee only if all of the following conditions have been met:

1) All subjects have finished their final research visits and enrollment is permanently closed with no prospect for further data collection or any continuing human subject interactions or interventions for the purpose of research; AND
2) If the study has a sponsor, either the sponsor or the sponsor representative has indicated in writing that the study is completed at the University and that study closure is requested or the Principal Investigator has withdrawn his/her participation in the sponsor's protocol and has given written notification of this withdrawal to the sponsor; AND
3) All data (including study follow-up data) pertaining to human subjects has been collected; AND
4) Data analysis of identifiable private information at the University is complete; AND
5) All study documents (e.g. adverse event reports, study deviations etc) have been reviewed. If any of these above conditions do not apply and/or if there is any new information about risk or subject safety included in the final report that was not previously reported and/or for any other reason the administrative designee believes appropriate, the final report shall be referred to the IRB chair or IRB designee for approval or deferral to the convened IRB.

If the final report is referred to the convened IRB, the panel shall decide among the actions indicated below:

1) **APPROVED:**
   The Principal Investigator shall be informed in writing by the HSRO. The determination letter shall inform the Principal Investigator of any IRB required actions and that study records must be retained for at least three years.

2) **DEFERRED:**
   With this decision, the IRB shall specify what action(s) needs to be taken and who has the authority for subsequent review including that of revised or requested materials. A memo shall be sent to the Principal Investigator by the HSRO indicating the specific action(s) required of the Principal Investigator. There must be full compliance with the required revisions and/or clarifications before the final report can be approved.
3) **TABLED:**
This motion shall result if the IRB is unable or unwilling to review and/or vote on a final report. This may occur if the quorum is lost, pertinent documents are unavailable or the scope of IRB expertise is not considered sufficient for appropriate decision-making. Although the Principal Investigator shall be notified of this motion by the HSRO, action may or may not be required by the Principal Investigator.

4) **DISAPPROVED:**
The final report is not approved by the IRB for reasons specified in a Letter of Disapproval to the Principal Investigator from the HSRO. The Principal Investigator may respond to the IRB with written justification for a reversal of the decision or a proposal to change the conditions underlying the final report which may be a basis for IRB reconsideration.

The Principal Investigator may request to attend a scheduled IRB meeting to discuss the disapproval.

If a Principal Investigator terminates employment or other association with the University, he/she must to submit a final report to the IRB or transfer the study to another Principal Investigator via an amendment which requires approval by the department chair and IRB. If the departing Principal Investigator is unwilling or unable to provide such an amendment, the academic department chair or the director of the University institute/center that provides oversight to the study may take such action or the HSRO may seek to administratively close the study.

A study may also be administratively closed by an IRB chair, an IRB-designee or an administrative-designee without a final report from the Principal Investigator if the Principal Investigator (or the department chair or University institute/center director in the case where a principal investigator is unavailable) affirms in writing to the HSRO that the study was never initiated after IRB approval and that no subjects were enrolled. If the study was sponsored, the Principal Investigator must also submit written documentation (letter or email) to the HSRO that:

1) The sponsor has notified the Principal Investigator that the study is being discontinued or closed; **OR**
2) The Principal Investigator has notified the sponsor that he/she no longer wishes to participate in the study and the study is being discontinued or closed. A copy of this notification should be provided by the Principal Investigator to the HSRO.
SECTION 13: SUSPENSION, TERMINATION AND ADMINISTRATIVE CLOSURE OF IRB APPROVED RESEARCH
13.1 **GENERAL PRINCIPLES**

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** April 24, 2007  
**Revised:** April 30, 2012

The IRB and/or members of University Administration (Executive Vice President and Provost, Vice Provost for Research, Associate Vice Provost for Human Subject Research, Associate Vice Provost for Research, Assistant Provost for IRB Affairs) have the authority to suspend, administratively close or terminate approval of human subject research studies (c.f. 45 CFR 46.113/21 CFR 56.113). Such "for cause" suspension or termination may be implemented by administrative action, expedited action or action of the convened IRB for reasons including that:

1) The research is not being conducted in accordance with University of Miami policies and/or procedures for research  
2) There is serious or continuing non-compliance with IRB requirements, IRB determinations or federal regulations  
3) A serious incident has occurred involving injury or any other serious unanticipated problem involving risk to subjects or others  
4) IRB approval has lapsed and the study is in suspension

[NOTE – The unmodified term "suspension" is commonly used to describe suspensions that occur “for cause” (as the result of an action by University administration or the IRB) and suspensions that occur automatically as the result of a lapse in IRB approval. Sections 13.2-13.4 of this policy pertain to "for cause" suspensions. Section 13.5 pertains to suspensions due to lapse in IRB approval.]

Any suspension for lapse in IRB approval or any suspension or termination for cause shall be documented by the suspending/terminating authority in writing with a statement of the reasons for this action. Notification of the suspension or termination shall be provided in a timely manner to the HSRO which shall be responsible for informing the principal investigator and appropriate institutional officials (including the Associate Vice Provost for Human Subject Research, the Vice Provost for Research and the Chair of the investigator’s academic department), and sponsoring agencies (if applicable). The Associate Vice Provost for Human Subject Research shall inform the Vice Provost for Research who will report the "for cause" suspension or termination to OHRP and/or the FDA (pursuant to 45 CFR 46.103(b), 45 CFR 46.113, 21 CFR 56.108(b) and 21 CFR 56.113) and to any applicable funding agency as required by the agency.

The communication to the principal investigator should explain the reasons for this action and the consequences of a suspension or termination. This letter should inform the principal investigator that he/she has an opportunity to appeal to the convened IRB about the suspension or termination. A Principal Investigator may appeal to the IRB about a decision to suspend or terminate a study. This
appeal must be made in writing within 10 working days following receipt of the written notice of suspension or termination unless these stipulations are waived by the Associate Vice Provost for Human Subject Research or the Chair of the IRB providing study oversight.

If the principal investigator chooses to appeal the suspension/termination to the convened IRB, the principal investigator should provide a plan for ensuring that the rights and welfare of all currently enrolled and previously enrolled participants are protected and a plan to ensure that future participants will be protected if the study receives IRB approval to continue.

**During a study suspension**, either "for cause" or due to lapse in IRB approval, new subjects may no longer be enrolled, and a decision as to whether currently enrolled subjects must continue to receive study-related interventions due to safety concerns shall be communicated to the Principal Investigator. Study interventions or interactions with already enrolled subjects should only continue when these are in the best interest and safety of individual subjects. Those authorized to make decisions on the safety of individual subjects are the Assistant Provost for IRB Affairs the IRB Chair or designee or the convened IRB who may seek information from the Principal Investigator as required. The decision on subject safety shall be forwarded to the HSRO for communication to the principal investigator.

For studies suspended "for cause", the IRB or suspending administrator shall consider the effect of the suspension on the rights and welfare of current participants and shall require that the principal investigator provide a plan outlining what action shall be taken for those participants currently enrolled in the study and how the participants shall be informed if applicable.

**If a study is terminated**, the IRB or terminating administrator must consider the effect of the termination on the rights and welfare of current participants. New subjects may not be enrolled and all study-related activities including interventions with currently enrolled subjects and data analysis must cease. The IRB or terminating administrator may require specific steps that must be taken by the Principal Investigator to implement the termination.

Whether a study is suspended or terminated by administrative, expedited or IRB action, the convened IRB shall determine and inform the HSRO which shall inform the principal investigator if other actions must be taken. Such actions may include:

1. Notifying currently enrolled subjects in writing that the study has been suspended or terminated. Written communications to subjects shall usually come from the Principal Investigator and must be reviewed and approved by the IRB prior to its distribution to subjects; however, the IRB may require that written communication be provided to subjects from another source such as the academic department chair or the HSRO. Such communication also requires approval by the IRB prior to its distribution to subjects.
2. Implementing procedures for withdrawal of subjects that consider the rights and welfare of those subjects
3. Informing subjects of any follow-up procedures permitted or required by the IRB for their safety

[NOTE – If decided by the IRB, this may be included in the communication notifying subjects of the suspension or termination –see above]
The lifting of a "for cause" suspension may not occur by expedited action but requires approval by the convened IRB and by the Associate Vice Provost for Human Subject Research. The lifting of a suspension for lapse of IRB approval shall occur upon approval of the continuing report either by expedited review/approval by the IRB Chair or designee (if the study meets the eligibility criteria for such review/approval) or by review and approval by the convened IRB.
13.2 **ADMINISTRATIVE ACTION**

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** April 6, 2006  
**Revised:** April 30, 2012

The suspension or termination of a study by administrative action may be taken if it is deemed immediately necessary to ensure the safety of human subjects. Such prompt action may occur upon determinations such as (but not limited to) that an alleged practice within a study:

1) Has or had risks to subjects or others; **OR**  
2) Constitutes serious or continuing non-compliance with IRB determinations or federal regulations

Administrative action to suspend or terminate a study may be implemented by the Executive Vice President and Provost, the Vice Provost for Research, the Associate Vice Provost for Human Subject Research, the Associate Vice Provost for Research or the Assistant Provost for IRB Affairs. Administrative suspension or termination of a study shall be immediately implemented upon notification to the Principal Investigator or other key personnel in the absence of the Principal Investigator. Principal Investigators shall be informed by letter from the HSRO about the action taken, its justification and any required steps for corrective action and/or closure. The action and its justification shall also be promptly reported to the convened IRB by the HSRO.
13.3 EXPEDITED ACTION

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: April 6, 2006
Revised: April 30, 2012

The suspension or termination of a study by expedited action may be taken if the IRB Chair or Chair-designee deems that such prompt action is necessary to ensure the safety of human subjects and that it is inappropriate to await action by the convened IRB. Such prompt action may occur if notification is received by the IRB or referred to the IRB by administration outside of a regularly scheduled IRB meeting. Reasons for expedited action may include that the alleged practices have or had the potential to:

1) Cause injury or any other unanticipated problems involving risks to subjects or others; OR
2) Constitute serious or continuing non-compliance with IRB determinations or federal regulations

As part of his/her review, the expediting reviewer may request an investigation by the Office of Research Support and Quality Assurance (RSQA) and/or may conduct an inquiry by requesting specific information from the Principal Investigator. Expedited suspension or termination of a study shall be immediately implemented upon notification to the Principal Investigator or other key personnel in the absence of the Principal Investigator. Principal Investigators shall be informed by letter from the HSRO about the action taken, its justification and any required steps for corrective action and/or closure. The action and its justification shall also be promptly reported to the convened IRB by the HSRO.
13.4 CONVENED IRB ACTION

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** April 6, 2006  
**Revised:** April 30, 2012

The convened IRB has the responsibility and the authority to suspend or terminate its approval of any study that it has reviewed and approved for reasons such as that the alleged practices of the study have or had the potential to:

1. Cause injury or any other unanticipated problems involving risks to subjects or others; **OR**  
2. Constitute serious or continuing non-compliance with IRB determinations or federal regulations

Such actions shall be incorporated into the minutes of the meeting. The IRB shall consider the rights and welfare of current research subjects when suspending or terminating approval of active studies.

As part of its review and deliberations, the IRB may request an investigation by the Office of Research Support and Quality Assurance (RSQA) and/or may initiate an inquiry by requesting specific information from the Principal Investigator. Suspension or termination of a study by IRB action shall be immediately implemented upon notification to the Principal Investigator or other key personnel in the absence of the Principal Investigator. Principal Investigators shall be informed by letter from the HSRO about the action taken, the reasons for the suspension or termination and any required steps for corrective action and/or closure.

The IRB has the authority to take actions other than suspension and termination to ensure subject safety (**c.f.** Policy 3.1). Actions that the IRB may take include, but are not limited to:

1. Requiring more frequent than annual review of a protocol  
2. Imposing a probationary period for an investigator  
3. Suspending an investigator’s right to perform studies, pending remedial action(s)  
4. Requiring that additional educational requirements be completed by the Principal Investigator and his/her staff  
5. Transferring responsibility for the protocol to another principal investigator  
6. Arranging for additional or alternate physician follow-up  
7. Arranging for the subject to remain in the study at another institution
13.5 SUSPENSION AND ADMINISTRATIVE CLOSURE FOR LAPSE IN IRB APPROVAL

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: April 24, 2007
Revised: April 30, 2012

If a continuing review of an active study is not approved prior to the end of the previously approved duration of the study, the IRB approval shall automatically expire and the study shall be suspended in accordance with federal regulations. The HSRO may provide warning notices of study expiration to Principal Investigators prior to the study expiration date, but investigators should understand that these are a courtesy and are not required. It is the responsibility of the Principal Investigator to monitor approval periods and to ensure that continuing reports are filed in ample time to allow for IRB review.

Letters informing the Principal Investigator of a suspension for lapse in IRB approval may be sent by the HSRO but these letters are also a courtesy to Principal Investigators who are responsible for suspending study-related activity, including subject accrual and other changes pursuant to regulations whenever IRB approval has lapsed.

Expiration of IRB approval will not be reported to OHRP. This is in contrast to the reporting that must occur pursuant to HHS regulations and OHRP guidance if a study is suspended or terminated for cause.

If a study has lapsed in IRB approval and the Principal Investigator wishes to continue the research, continuing reports should be submitted immediately but in no case should a continuing report be submitted to the HSRO later than 45 days after the lapse in IRB approval. During the suspension for lapse in IRB approval, initial (i.e. new) studies from the Principal Investigator may be submitted and the IRB may review and approve such studies, but the IRB has the authority to make implementation of the new study contingent upon approval of either a continuing report or a final report (or administrative closure) for the suspended study.

If a study suspension for lapse in IRB approval extends beyond 90 days, the study shall be administratively closed unless this closure is waived by the Associate Vice Provost for Human Subject Research. This administrative closure shall be reported to the IRB and the Chair of the Principal Investigator’s academic department. If two studies from a Principal Investigator are administratively closed within a 3-year period, the IRB shall review the circumstances and make recommendations regarding corrective action.
13.6 VOLUNTARY SUSPENSION BY THE PRINCIPAL INVESTIGATOR OR TEMPORARY WITHHOLD BY THE INSTITUTION

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: June 1, 2008
Revised: April 30, 2012; June 5, 2012

In addition to the actions described above, an IRB-approved study may be voluntarily suspended upon request by the Principal Investigator of that study. The Associate Associate Vice Provost for Human Subject Research may also temporarily withhold permission for a Principal Investigator to conduct a study at any time. Voluntary suspensions and temporary withholds shall be governed by the policies on suspensions defined in this SECTION 13 of the IRB Written Policies and Procedures with regard to enrollment, subject safety, the continuance of treatments, and the collection, evaluation and use of research data and information. These policies include that subject enrollment must cease and that study interventions or interactions with already enrolled subjects should continue only when these are in the best interest and safety of individual subjects as determined by those authorized to make such decisions.

Requests for voluntary study suspension should be directed to the HSRO in writing. Voluntary suspensions require approval by the Associate Associate Vice Provost for Human Subject Research or his designee. Approval of a suspension volunteered by the Principal Investigator is subject to the stipulation that lifting of the voluntary suspension by Principal Investigators must be preceded by written notice to the HSRO at least one full working day prior to the resumption of study activities and/or enrollment. A voluntary suspension of enrollment and/or other study activities by the Principal Investigator without administrative suspension shall not be defined as a "suspension" as per definition in other policies in this section and shall not carry with it the reporting requirements of a suspension for cause.

If the Associate Associate Vice Provost for Human Subject Research temporarily withholds study permission or subsequently reinstates such permission, he/she must inform the Principal Investigator and the HSRO promptly in writing. Such temporary withholds by the Institution shall also not carry the reporting requirements of a suspension for cause, since the withdrawal of permission is temporary and must be unrelated to compliance with human subject research-related federal regulations or UM IRB policies and determinations.
A voluntary suspension shall not be approved for a study that is already in suspension either by administrative action or by determination of the IRB. However, a study under voluntary suspension may be suspended either by administrative action or by IRB determination. If a suspension "for cause" is imposed administratively or by the IRB, this suspension shall override the voluntary suspension or temporary withhold of permission by the Institution and carry with it the reporting requirements defined in other policies in this section.
SECTION 14: UNANTICIPATED PROBLEMS AND ADVERSE EVENTS
14.1 PROBLEMS AND EVENTS THAT REQUIRE PROMPT REPORTING

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: April 27, 2006
Revised: June 1, 2012

1. ADVERSE EVENT or PROBLEM

Federal documents and professional literature interchangeably refer to a “problem” or an “adverse event” as any undesirable physical or psychological experience to or within a human subject participating in research (NOTE: FDA regulations define adverse events as any undesirable experience associated with the use of a medical product in a patient).

2. INTERNAL VS EXTERNAL

Federal guidance differentiates between problems/ events that are “internal” (i.e. experienced by a research subject enrolled at a site under the jurisdiction of the University of Miami IRB for either multicenter or single center research projects) or “external” (i.e. experienced by subjects enrolled at a site external to the jurisdiction of the University of Miami IRB or in a study for which UM is not the coordinating center).

3. RELATED

An event is “related” if it is likely to have resulted from participation in the research study

4. SERIOUS ADVERSE EVENT

Federal regulations consider an adverse event to be serious when medical or surgical intervention is required to prevent any of the following:

   i. Death
   ii. A life-threatening situation
   iii. Inpatient hospitalization
   iv. Prolongation of existing hospitalization
   v. A persistent or significant disability/incapacity, or congenital anomaly/birth defect

Pursuant to federal regulations, adverse events that do not result in death or are not life threatening or require hospitalization should also be considered serious adverse events when, based upon appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.
5. **UNANTICIPATED**

An event is unanticipated if it was unforeseeable at the time of its occurrence (i.e. it is not consistent with the current Investigator’s Brochure; or if an Investigator’s Brochure is not required or available, the event should be considered unanticipated if its specificity or severity is not consistent with the risk information described in the investigational plan or elsewhere in the IRB application. Note- if adverse events occur at a greater frequency, severity or duration that was previously anticipated, these events should be considered “unanticipated” and must be promptly reported.

6. **UNANTICIPATED PROBLEMS INVOLVING RISK TO PARTICIPANTS OR OTHERS**

This defines any event that was:

1) Unanticipated
2) Related
3) Places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized

Examples of such unanticipated problems include but are not limited to:

a) Breach of confidentiality
b) Loss of research data stored without encryption
c) Any change to the protocol made without prior review even if done to eliminate an apparent immediate hazard to subjects
d) Subject complaints that indicate unexpected risks
e) Sponsor-imposed suspensions

*NOTE:* Unanticipated problems involving risk to participants or others should be reported to the IRB regardless of whether the problems occur during the study, after study completion, after participant withdrawal or after study closure.
14.2 DEFINITIONS

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: April 27, 2006
Revised: June 1, 2012

14.2(A) PROMPT REPORTING (10 DAYS)
Pursuant to federal regulations (45 CFR 46.103(b)(5) and 21 CFR 56.108(b)(1), problems (adverse events) which fit all of the following three criteria must be promptly reported to the IRB (and to sponsors and/or a central or independent monitoring committee [i.e. DSMB] as applicable).

Unless otherwise defined, “prompt reporting” should be made via the HSRO’s “Reportable Event” form within 10 working days after the investigator first learns of the problem (adverse event).

The criteria for prompt reporting are:

1) a) the problems (adverse events) are unanticipated (either in frequency, type, severity, scope or consequences) from the nature of the research procedures and the subject population being studied; OR

   b) the problems (adverse events) are expected but not fully addressed or specified in information provided to the IRB or to participants such as in the initial application or amendments, investigator brochures, scientific literature, product labeling, package inserts, IRB-approved informed consent documents or any existing documentation regarding the research conducted to date under the protocol); AND

2) the problems (adverse events) are related, or have a reasonable possibility of being related, to the research procedures or to the subject’s participation in the research; AND

3) the problems (adverse events) suggest that the research places subjects or others at greater risk of harm or discomfort than was previously known or recognized

One key to the above policy is “unanticipated”. Problems that are anticipated (e.g. in a high risk sample or in high risk research) do not necessarily require prompt reporting. But if such events are occurring at a significantly higher frequency or severity than expected, they constitute an unanticipated problem and must be promptly reported.
Another key to the above policy is that a problem need not directly affect a subject to require prompt reporting. For example, the loss of a computer containing identifiable and sensitive subject information must be promptly reported as an **unanticipated problem**. Other examples of unanticipated problems which must be promptly reported include but are not limited to:

a) findings that lab reports on blood or other samples were in error  
b) a drug dosing error  
c) hospitalization (initial or prolonged) due to (or possibly due to) the adverse event  
d) disability (i.e. a subject underwent a significant, persistent or permanent change, impairment, damage or disruption of bodily function/structure, physical activities or quality of life, which is related or possibly related to participation in the study)  
e) congenital abnormality (i.e. the suspicion that exposure to a medical product prior to concept or during pregnancy resulted in or contributed to an adverse outcome in a child  
f) required intervention to prevent permanent impairment or damage (i.e. there is a suspicion that the use of a medical product resulted or may result in a condition requiring medical or surgical intervention to preclude permanent impairment or damage to a subject  
g) a research participant unexpectedly becomes pregnant in a study that includes interventions that may adversely affect pregnancy and/or pregnant women  
h) cessation of an investigational behavioral intervention  
i) inadvertent disclosure of confidential information (note—these are “serious” if they present an immediate risk to subjects such as from spousal or child abuse)  
j) an important medical event that jeopardizes the subject or requires medical intervention to prevent one of the outcomes listed above  
k) physical abuse for participating in the research  
l) unexpected violence by participants in a group counseling session

Federal regulations and IRB policies also require prompt reporting in each of the situations defined below:

1) any unanticipated adverse device effects occurring during the research (note – this must be reported to the HSRO and to the sponsor [if applicable] as soon as possible but no later than 10 working days after the investigator learns of the problem.. The sponsor shall immediately conduct an evaluation of the unanticipated device problem [21 CFR 812])

2) any unanticipated internal drug problem associated with an IND-covered study (note – this must be reported to the HSRO and the sponsor [if applicable] within 10 working days after the investigator first learns of the occurrence. The sponsor shall notify the FDA and all participating investigators in a written IND safety report [21 CFR 312]

3) any problem (even if it does not constitute an “unanticipated problem” by the definition above) if the protocol defines that problems (adverse events) are to be reported to a DSMB *(NOTE: such problems must be reported to the DSMB and HSRO within 10 working days after the investigator first learns of the occurrence)*
14.2(B) **SUBJECT DEATH**

The unanticipated death of a subject must be reported within 24 hours if that death is suspected as being a direct outcome or possibly an outcome of the study intervention (If the cause of death is not available, this should not delay the report)

Reporting of a subject’s death is required only at the time of continuing review if that death fits any of the following criteria:

a) The death of a subject is due to the nature of the subject’s underlying disease or condition, or is identified as due to a possible risk of the study procedure/intervention as described in the protocol and consent form

b) the death of a subject occurs more than 30 days after she/he has stopped or completed all study procedures/interventions and required follow-up

c) the death is that of a subject who did not complete the protocol for whatever reason, including voluntary withdrawal or removal by the PI

d) the death is that of a subject participating in a study which does not include a research intervention (for example, an observational study tracking outcomes)

14.2(C) **LIFE THREATENING PROBLEM**

A problem (adverse event) that is life-threatening must be reported within 24 hours. Federal guidance defines “life-threatening” as being when a subject was at substantial risk of dying at the time of the problem or it is suspected that the use or continuance of the intervention/drug/device would result in the subject’s death
14.3 REVIEW OF PROBLEMS OR EVENTS THAT REQUIRE PROMPT
REPORTING

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: August 27, 2007
Revised: June 1, 2012

Pursuant to policy 14.2, Principal Investigators must promptly report certain problems (adverse events) to the HSRO via the “Reportable Event” form in ePROST and to the sponsor and/or a central or independent monitoring committee (e.g., DSMB) as applicable. Within these reports, the principal investigator shall assess the cause and seriousness of the problem (adverse event) and advise whether:

a) a change in the protocol is necessary to minimize the risks to subjects
b) the consent form should be revised to reflect the risk, and
c) subjects in the study should be re-consented in light of the risk.

The HSRO shall promptly forward the principal investigator’s report to the IRB Chair or designee. If immediate risks to subjects are involved, the report shall be forwarded to the Associate Vice Provost for Human Subject Research or the Assistant Provost for IRB Affairs or designees. Any of the above individuals may take one or more actions which may include (but are not limited to):

1) Implement immediate suspension of IRB approval to ensure the ongoing safety of subjects
2) Call an emergency meeting of the convened IRB to act upon the report
3) Request additional information from the Principal Investigator or others

All actions of the Associate Vice Provost, Assistant Provost, IRB Chair or designee regarding reportable problems or events shall be communicated to the Principal Investigator in writing and reported to the convened IRB.

Problems (adverse events) that fit the criteria for prompt reporting but that do not appear to require immediate action may be reviewed in an expedited manner by the IRB Chair or designee who may defer this review to the convened IRB when deemed appropriate. Expedited review shall be limited to reported problems (adverse events) where only slight changes in risk have been reported, such that only minor changes in the study protocol or informed consent documents are required. The IRB Chair or designee or the convened IRB may ask investigators and/or Data Safety Monitoring Boards or others for additional clarifying information and may require remedial actions (which shall be reported to the Principal investigator in writing) which may include:

1) Modifying the inclusion or exclusion criteria to mitigate the newly identified risks
2) Implementing additional monitoring procedures of subjects
3) Modifying informed consent documents to include a description of newly recognized risks
4) Revising the protocol
5) Providing additional information about newly recognized risks to previously enrolled subjects
6) Suspending enrollment of new subjects
7) Suspending approval of the research
8) Terminating approval of the study (convened IRB only)

Amendments submitted by Principal Investigators in response to reported problems (adverse events) shall be reviewed pursuant to policies governing reviews of other amendments.

The Associate Vice Provost for Human Subject Research shall be responsible for promptly communicating in writing to appropriate institutional officials including the Executive Vice President and Provost, the Dean of the School/College, and the Vice Provost for Research details and corrective actions or plans (as applicable) of:
  a) any reported problems (adverse events) involving risks to subjects or others;
  b) any serious or continuing noncompliance with 45 CFR part 46 or the requirements or determinations of the IRB; and
  c) any suspension or termination of IRB approval pursuant to the policies defined in Section 13.

The Vice Provost for Research shall be responsible for promptly communicating in writing to supporting departments or agency heads (or designees) and the OHRP and/or FDA the details and corrective action plans related to any unanticipated problems involving risks to subjects or others; any serious or continuing noncompliance with 45 CFR 46, 21 CFR 56 or the requirements or determinations of the IRB and any suspension "for cause" or termination of IRB approval pursuant to the policies defined in Section 13.

**NOTE:** Reportable external problems (adverse events) need not be communicated by investigators to the UM IRB if UM is not the coordinating site in a multi-center study.

**NOTE:** If problems occur at a non-UM (or non-UM affiliated) site at which a UM investigator is responsible for the conduct of the research but the UM IRB does not serve as the IRB of record for that research, those problems need not be reported to the UM IRB unless the problem/event is unanticipated, related and places subjects at a greater risk than was previously known.
14.4 REPORTABLE PROBLEMS/EVENTS AT CONTINUING REVIEW

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: April 27, 2006
Revised: June 1, 2012

Internal problems/adverse events that do not require prompt reporting to the IRB (per criteria defined in Section 14.3 of these policies) must be submitted as a summary of events with an assessment of risk within the continuing report.

Although “internal” problems (adverse events) requiring prompt reporting pursuant to the criteria of 14.2 (above) should already be known to the IRB, applications for study continuance at the time of continuing review must also include a summary of those problems (adverse events). For “external” problems (adverse events) from multi-center studies, the Principal Investigator must include with the continuing report:

1) the most recent copy of the sponsor’s analysis of the problems (if applicable)
2) the most recent copy of the Data Safety Monitoring Board report if received by the Principal Investigator from a DSMB (NOTE: The IRB may request DSMB reports from sponsors if these are not available to the Principal Investigator).
3) a summary of all external unanticipated problems presented in the context of the entire multi-center study, if possible.
14.5 EXTERNAL ADVERSE EVENTS AND SAFETY NOTICES/REPORTS FROM SPONSOR OR CENTRAL SITE

Review Responsibility: IRB Policy and Procedure Committee
Original Approval Date: November 28, 2007
Revised: June 1, 2012

This policy pertains to external problems (adverse events) or other materials emerging from sites other than the University of Miami or affiliated institutions within multicenter studies in which UM is engaged.

A general principle is that investigators at all participating institutions within multicenter studies should learn of external problems (adverse events) that require prompt reporting via reports that are distributed by the sponsor, coordinating center or data safety monitoring committee. Summary reports generated by the sponsor and/or data monitoring committee (when applicable) should be submitted for review at the time of study continuation.

External events that do not meet the criteria of unanticipated problems and have no effect on the risks to subjects participating at UM do not require reporting to the UM IRB. External problems that are unanticipated and increase risk to subjects who are participating locally (i.e. they require a change in the protocol or consent documents) or that occur in studies in which UM is the prime awardee or coordinating center in a multicenter study should be reported to the UM IRB within 10 calendar days of their becoming known. Changes in the protocol or consent forms that occur in response to external problems should be submitted to the UM IRB as amendments.

External unanticipated problems that occur in clinical trials sponsored by cooperative groups (RTOG, COG etc) do not require reporting to the UM IRB.

14.5(A) SAFETY NOTICES, INFORMATIONAL ITEMS AND REPORTS:

Federal regulations do not require that safety notices or other informational items or reports from sponsors or a non-UM coordinating center in a multi-site study be submitted to the IRB.

UM principal investigators should maintain copies of external unanticipated problem reports, safety notices and related materials which shall be made available to the IRB upon request.
SECTION 15 STUDY VIOLATIONS
15.1 STUDY VIOLATIONS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: July 24, 2006

A study violation (also commonly referred to as a study or protocol deviation) is defined as an unplanned or unforeseen failure by the Principal Investigator or other study personnel to follow the specified procedures approved by the IRB for the study. Such violations often represent non-compliance and they differ from amendments since they usually apply to only a single occurrence or subject and are not intended at the time to modify/change the study.

It is the responsibility of the Principal Investigator to determine which is applicable between the two general categories of study or protocol violations/deviations:

1) Major Violations/Deviations:

These are violations that may impact subject safety, condition or status, affect the integrity of study data, pose a significant risk of harm and thereby change the risk/benefit ratio and/or affect a subject's willingness to participate in the study. Examples of major violations include (but are not limited to):

- Failure to obtain informed consent
- Informed consent was obtained after initiation of study procedures
- Informed consent for IND/IDE studies was obtained by someone other than individuals authorized by the IRB to obtain consent
- Enrollment of a subject who did not meet all inclusion/exclusion criteria
- A study procedure was performed without IRB approval
- Failure to report a serious adverse event to the IRB and sponsor
- Failure to perform a required lab test
- Drug/study medication dispensing or dosing error
- Study visit conducted outside of the required timeframe
- Failure to follow the safety monitoring plan

Major study violations must be reported by the Principal Investigator to the HSRO and to the sponsor (if applicable) as outlined in the sponsor’s protocol within 10 working days of discovery with the exceptions that:

Study violations that have resulted in the death of a subject or a life-threatening event, even if anticipated, must be reported to the IRB pursuant to the "serious adverse events" policy within 24 hours of the knowledge of the event. If the cause of death is not available, this should not delay the reporting of the event.
The HSRO shall screen reports of major study violations to determine if immediate action is required and then forward the report for review to the IRB Chair or designee who shall determine whether immediate and/or further action is required, whether minimal risk changes in the study protocol or informed consent documents are required and/or whether the report should be deferred to the convened IRB. If immediate action is recommended by the HSRO staff or the IRB Chair/designee, the report shall be forwarded either by the HSRO to the Associate Vice Provost for Human Subject Research or the Assistant Provost for IRB Affairs or to the IRB Chair or designee who may take one or more actions which may include (but are not limited to):

a. Implement immediate action to ensure the ongoing safety of research participant
b. Call an emergency meeting of the convened IRB meeting to act upon the report
c. Present the report to the convened IRB at the next scheduled meeting
d. Request additional information from the Principal Investigator or others
e. Require establishment of a monitoring committee or the involvement of another entity to ensure subject safety

Reports of major study violations not requiring immediate action shall be reviewed by the IRB Chair or designee who may defer this review to the convened IRB when deemed appropriate. The IRB Chair or designee or the convened IRB may ask investigators and/or Data Safety Monitoring Boards for additional clarifying information and may require modifications to the protocol and/or consent documents if it is apparent that risks are greater than those originally stated. The IRB may suspend or terminate a protocol if these actions are required to eliminate untoward risks to human subjects. All changes to the protocol or consent documents must receive prior approval by the IRB before implementation.

All actions of the IRB Chair or designee regarding study violations shall be reported to the convened IRB. All actions of the IRB Chair or designee and/or the convened IRB shall be promptly communicated to the Principal Investigator in writing.
2) **Minor Violations/Deviations:**

These are violations that may not impact subject safety, compromise the integrity of study data and/or affect a subject's willingness to participate in the study. Examples of minor violations may include (but are not limited to):

- Implementation of unapproved recruitment procedures
- Missing pages of executed consent form
- Inappropriate documentation of informed consent, including missing signatures of a subject or investigator
- Consent form copy not given to the person signing the form
- Someone other than the subject dated the consent form
- Use of invalid consent form, i.e. consent form without IRB approval stamp, or outdated/expired consent form
- Failure to follow the approved study procedure that, in the opinion of the PI, does not affect subject safety or data integrity
- Study procedure conducted out of sequence

Principal Investigators are cautioned that the above examples listed as possibly being "minor violations/deviations" may, in some circumstances, impact on subject safety, or affect a subject's willingness to participate in the study. If these circumstances apply, then the violations/deviations must be considered to be "major" and must be reported by the Principal Investigator to the HSRO pursuant to the policy on "major violations/deviations" (see above).

Minor violations shall be reported by the Principal Investigator with the continuing review.
SECTION 16: COMPLIANCE AUDITS
16.1 GENERAL PRINCIPLES

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: December 20, 2005

A strategy for ensuring and improving the quality of the human subjects protection program is the implementation of an internal audit process. This is because an audit process can heighten investigator and IRB awareness of regulatory requirements and improve the ethical conduct of research. Authority for a research audit program is derived from federal regulation 45 CFR 46.109(e) and 21 CFR 56.109(f) which state that “an IRB … shall have the authority to observe or have a third party observe the consent process and the research.”

At the University, the “third party” is the Office of Research Compliance Assessment, which is supervised by the Vice Provost for Research. This Office has responsibility for:

1) Investigating allegations of non-compliance with federal and other regulations
2) Investigating allegations of non-compliance with the requirements or determinations of the IRB
3) Conducting audits to ensure that there is compliance with regulations and IRB decisions

Such investigations, whether routine or directed, shall have the involvement and/or consultation of the IRB and HSRO. The Associate Vice Provost for Human Subjects Research, or the Assistant Provost for IRB Affairs may also request an audit by the Office of Research Compliance Assessment as may the IRB of any study it has approved. The request may be made by the full IRB or by the Chair or the Chair's IRB-designee at his/her discretion. The Office of Research Compliance Assessment may also initiate audits. Studies may be routinely chosen for audit or they may be selected for audit by predetermined criteria based on assessment of risk or they may be chosen for a particular reason such as funding source, number or type of studies being done by any one principal investigator or because the studies involve vulnerable populations. Investigators are expected to cooperate fully with the auditors.

When made aware that a routine or directed audit is being undertaken by the Office of Research Compliance Assessment, no matter whether this audit is being conducted on a routine basis or in response to an allegation or problem requiring an audit, the HSRO shall compile file information and any other documentation and make these available to the officers of the Office of Research Compliance Assessment. The IRB and HSRO shall have full and ongoing access to information pertaining to audits conducted by the Office of Research Compliance Assessment. The IRB may also conduct its own inquiry or request materials/meetings in order to contribute to the investigation being conducted by the Office of Research Compliance Assessment.
If warranted by findings of serious non-compliance or practices that may immediately jeopardize the safety and welfare of human subjects, the Office of Research Compliance Assessment shall contact the Associate Vice Provost for Human Subjects Research before the audit is complete or before a response is requested from the Principal Investigator. The Associate Vice Provost for Human Subjects Research may take any or all actions deemed necessary and within his/her authority (c.f. Policy 3.2) including suspension or termination of the study.

The Office of Research Compliance Assessment shall document the outcome of its audits including communications, discussions and efforts to achieve resolution in writing, by either e-mail or paper memo with a copy to the files. Such documentation shall be factual and objective, and may include timelines for resolution if appropriate (e.g. meeting dates, response deadlines). All audits shall be reported to the IRB. If the documentation reveals non-compliance, this documentation shall be quickly forwarded to the HSRO for review by the IRB chair or IRB-designee who shall determine whether the practices cited in the report constitute relatively minor non-compliance or whether the practices may constitute serious or continuing non-compliance that may cause injury or any other unanticipated problems involving risks to subjects or others and/or that may adversely affect the rights, safety and/or welfare of human research subjects.

If the non-compliance is determined to be serious or continuing based on the definition above, the IRB Chair or designee shall forward the report for review and action by the convened IRB. If the IRB Chair or designee determines that there are serious or continuing non-compliance or practices that may immediately jeopardize the safety and welfare of human subjects, the IRB Chair or designee shall also contact the Associate Vice Provost for Human Subjects Research without waiting for review by the convened IRB.

If the IRB chair or IRB-designee forwards the audit report to the full IRB, the IRB may request that staff of the Office of Research Compliance Assessment and/or the staff of the HSRO and/or the principal investigator or other key personnel provide information at the meeting. The IRB shall review the audit findings and determine by vote whether there shall be required corrective actions or sanctions which should be systematic in nature and may include (but are not limited to):

1) Additional, focused compliance audits
2) Suggestions or requirements for additional education/training in human subjects protections and regulations for investigators, staff and/or departments
3) Designating an IRB member or mentor to discuss compliance or other issues/concerns with the principal investigator
4) Notification to current or past participants of any modifications to the protocols or informed consent documents made in response to the audit
5) Modify the research protocol, consent process or consent documents
6) Send a letter of reprimand from the IRB to the principal investigator and/or recommend that a letter of reprimand be sent by the Associate Vice Provost for Human Subjects Research or the Provost
7) Termination or suspension of the research
8) Modify the continuing review timetable to require more frequent IRB review
9) Restrictions or disallowance on serving as an investigator in studies involving human subjects
10) Require the principal investigator to submit a corrective action plan to the IRB for review and approval
11) Noting that the audit served as an educational tool and that, based on the principal investigator's response to the audit, no further action is required

Following IRB review, the principal investigator shall be notified by the HSRO of the IRB decision. The principal investigator may submit a written request asking the IRB to reconsider its decision. The request should clearly indicate the facts or the interpretation in dispute and should provide supporting evidence where applicable. If a written request is received by the IRB, the IRB shall vote either to leave its decision unchanged or to reopen its review.

It is the responsibility of the IRB to ensure that changes and other mandates of the IRB are carried out by the principal investigator. To accomplish this, the IRB may request appropriate documentation from the principal investigator and/or the IRB may request that confirmatory site visits be performed, and reports made to the IRB, by the Office of Research Compliance Assessment or the HSRO.
16.2 REPORTING AUDIT FINDINGS AND OUTCOMES

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 27, 2009
Revised: March 18, 2012

Pursuant to regulations [45 CFR 46.103(a) and 45 CFR 46.103(b)(5)] and in accordance with the terms of the UM FWA, the Associate Vice Provost for Human Subjects Research will inform the Vice Provost for Research in writing of such matters that require reporting. The Vice Provost for Research shall report to the Office of Human Research Protections (OHRP):

1) Unanticipated problems involving risks to human subjects or others;
2) Any serious or continuing non-compliance with federal regulations or the requirements or determinations of the IRB
3) All study suspensions [with the exception of those that occur as the result of lapses of IRB approval] or terminations of IRB approval

Pursuant to regulations [21 CFR 56.108(b)] and in accordance with the terms of the UM FWA, the Vice Provost for Research shall report any of the following events involving FDA regulated products to the FDA:

1) Unanticipated problems involving risks to subjects or others
2) Serious or continuing non-compliance with federal regulations or IRB determinations or requirements
3) Any suspension [with the exception of those that occur as the result of lapses of IRB approval] or termination of IRB approval

The above events shall be reported to the FDA as follows: a) Division of Scientific Investigations (for drug products); b) Bioresearch Monitoring Branch (for biologic products); c) Division of Bioresearch Monitoring (for medical devices).

The Vice Provost for Research shall also report to the OHRP or FDA as appropriate any findings of serious or continuing non-compliance by the IRB. All reports to the OHRP and/or FDA shall be made promptly depending on the seriousness of the non-compliance. Investigations or implementation of corrective actions need not be completed prior to the reporting of non-compliance. If a report is provided prior to the completion of an investigation or the implementation of a corrective action plan, the Vice Provost shall provide a follow-up report to include the latter information.
Although regulations do not define “serious” or “continuing”, the IRB shall advise the HSRO when they believe that non-compliance with IRB determinations or federal regulations is “serious or continuing”. Examples of non-compliance that shall be considered 'serious' by the IRB, the Associate Vice Provost for Human Subject Research and the Vice Provost for research shall include but not be limited to the following:

1) Non-compliant actions that increase risk to participants and/or adversely affect their rights and welfare
2) Non-compliance that has harmed research participants or that may cause injury (physical, psychological, emotional etc)
3) Non-compliance that has compromised privacy and confidentiality of research participants or ethical principles
4) Non-compliant actions that decrease potential benefits or compromise the integrity or validity of the research
5) Conducting non-exempt human subject research without IRB review and approval
6) Substantive modifications to IRB-approved research being carried out without IRB approval
7) Enrollment of subjects who fail to meet the inclusion or exclusion criteria of the protocol resulting in increased risk to the subject
8) Enrollment of research subjects while study approval has lapsed
9) Enrollment of research subjects without approved informed consent
10) Willful or knowing misconduct by the principal investigator or key personnel

Examples of non-compliance that shall be considered 'continuing' by the IRB, the Associate Vice Provost for Human Subject Research and the Vice Provost for Research shall include but not be limited to the following:

1) Repeated instances of failure to follow federal regulations and/or IRB policies and procedures particularly after the IRB has informed the principal investigator and his/her key personnel of the problem(s) and that corrective actions needs to be taken
2) The principal investigator has multiple problems with non-compliance over a long period of time or has a problem with multiple existing or previously approved studies
3) A pattern of minor non-compliances with multiple studies by the same investigator(s) that reflect a lack of knowledge, unwillingness or a lack of commitment by the investigator and/or study team that, if unaddressed, may compromise the integrity of the human research or the protection program
4) Actions that suggest a likelihood that non-compliance will continue without intervention

In addition to federal agencies as required, serious or continuing non-compliance shall be reported by the Vice Provost for Research to the Dean(s) and academic department chair(s) of the Principal Investigator and other key faculty members involved in the research, to the Executive Vice President and Provost of the University and, if applicable, to the sponsors of the studies in which such non-compliance occurred.
SECTION 17: DATA SAFETY MONITORING BOARDS
17.1 DATA SAFETY MONITORING BOARDS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: August 3, 2009

All studies submitted to the IRB for review must contain a plan for adequately monitoring the data collected to ensure the safety of subjects [c.f. 45 CFR 46.111(a)(6) and 21 CFR 56.111(a)(6)]. Elements of data safety and monitoring plans may vary depending on potential risks, study complexity and type, but all plans must be suitable for the level of risk to be faced by subjects and to the nature of the research involved. If a study is sponsored by an agency or organization which requires specific data and safety monitoring standards, a copy of these monitoring standards must be attached to the study application and the Principal Investigator must submit to the IRB a plan to meet these standards.

For any study considered by the IRB to involve greater than minimal risk to human subjects, the IRB may require that the data safety and monitoring plan include a Data Safety Monitoring Board (DSMB). In particular, the IRB may (and usually will) require a DSMB for Phase III multi-site clinical trials involving interventions that entail potential risk to the participants.

In determining whether a DSMB is required, the IRB shall consider factors suggesting that a DSMB is needed which include:
   1) a large study population
   2) multiple study sites (since it is difficult to recognize unusual problems or patterns of problems when investigators are treating only a fraction of the participants)
   3) highly toxic therapies or dangerous procedures
   4) high expected rates of morbidity or mortality in the study population
   5) high change of early termination of the study especially if there is a reasonable likelihood that the study may be terminated early for reasons of safety, futility or efficacy

DSMB members should be experts in the scientific field of the study who are independent from the study and who may, at the discretion of the IRB, be internal or external to the institution. DSMB members shall have no professional or financial interest in the outcome of the studies they monitor. The DSMB shall function as an independent committee to monitor data throughout the duration of the study to determine if continuation of the study is appropriate scientifically and ethically. Determinations by the DSMB shall be considered as recommendations to the IRB and must be reported by the Principal Investigator to the IRB (through the HSRO) in a timely manner.
SECTION 18: ANCILLARY COMMITTEES
18.1 SYLVESTER COMPREHENSIVE CANCER CENTER PROTOCOL REVIEW COMMITTEE (PRC)

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** February 24, 2006

All studies involving human subjects that may be included within the definition of "oncology-related clinical trials" must be reviewed and approved by the Protocol Review Committee (PRC) of the University of Miami's Sylvester Comprehensive Cancer Center (SCCC). The SCCC functions as a matrix cancer center in the University of Miami's Miller School of Medicine.

The Protocol Review Committee of the SCCC serves as an evaluating body for the scientific quality of cancer-related studies, involving therapy and/or prevention. PRC review and approval are a prerequisite to consideration by the IRB. In this regard, the PRC functions as a required "ancillary committee" and the policy applies that studies may not be submitted to the IRB until all applicable "ancillary committee" approvals have been given.

The PRC is charged by the SCCC with the responsibility to ensure that studies conducted under the auspices of the SCCC meet peer-review standards for scientific rationale, specific aims, study endpoints and design, proposed analysis, ability to accrue subjects, adverse event reporting requirements, and plans for data and safety monitoring. The PRC reviews all proposed clinical trials for scientific merit with the exception of those designated as exempt on the basis of external peer review, such as those sponsored by designated cooperative groups.

The PRC also assigns a level of risk (low, moderate or high) to institutional trials that will be monitored internally by the Data and Safety Monitoring Committee (DSMC). This risk rating determines the frequency of DSMC review. The PRC also determines any exceptional requirements for specialized expertise in conducting DSMC reviews.

The requirement for PRC review/approval applies to (but is not limited to) all prospective, therapeutic trials that involve interventions such as chemotherapy, surgery, radiation therapy, immunotherapy, gene therapy, hormonal therapy, complementary therapy, or any combination thereof for which a UM faculty member serves as principal investigator.

The requirement for PRC review/approval does not apply to studies involving human subjects when these studies have only a behavioral or rehabilitative intervention. The policy also does not apply to studies that involve solely quality of life outcomes from standard therapies.
SECTION 19: EXTERNAL IRB'S
19.1 THE CENTRAL IRB (CIRB) OF THE NATIONAL CANCER INSTITUTE

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: April 20, 2007

19.1(a) GENERAL PRINCIPLES
In consultation with the Department of Health and Human Services Office for Human Research Protections (OHRP), the National Cancer Institute implemented a Central IRB (CIRB). This is designed to reduce the administrative burden on local IRBs and investigators while continuing a high level of protection for human research participants. Use of the CIRB facilitated review mechanism is available to investigators seeking to enroll subjects into adult and pediatric, national, multi-center (Cooperative group) cancer treatment trials.

The Adult CIRB has been meeting twice monthly and reviewing clinical trials since January 2001. The Adult Board currently reviews all Phase 3 Cooperative Group trials from the ACOSOG, CALGB, ECOG, GOG, NCCTG, NCIC, NSABP, RTOG, and SWOG, as well as any other studies opened in the Cancer Trials Support Unit (CTSU). The Pediatric CIRB was constituted in June 2004 and began meeting in November 2004. It reviews all NCI-approved COG Phase 2, 3, and Pilot protocols. Both Boards are composed of individuals who represent a broad range of oncology scientific and nonscientific disciplines.

The NCI CIRB processes are incorporated into the UM IRB policies and procedures per approval by both organizations. This permits participating investigators to log into the CIRB website and submit studies for CIRB review as outlined in the NIC CIRB Operations Office Standard Operating Procedures. The CIRB may take one of the following actions for each study: approve, approve pending modification, table or disapprove. After approval or disapproval, the Study Chair of the Cooperative Group shall be formally notified.

For each study, the CIRB’s primary reviews, minutes, notification letters, and any other correspondence are posted in its web site for participating institutions to access.

In addition to conducting initial reviews, the CIRB conducts Continuing Reviews and reviews of Serious Adverse Events (SAEs), Data Safety Monitoring Board (DSMB) reports, protocol amendments, national subject recruiting materials, etc. These actions are also posted on the CIRB web site for access by participating institutions.
19.1(B) UM REVIEW PROCEDURES PRE- AND POST- CIRB REVIEW

In addition to UM IRB requirements, policies of the UM Sylvester Cancer Center (SCCC) must be followed in the submission of studies, amendments, continuing reports and other items for CIRB approval (see above). In brief, investigators must receive approval from the SCCC Protocol Review Committee prior to submitting the study or other items to CIRB. Once the SCCC-PRC has approved, the study or item may be submitted to CIRB and a “short-form” version of the study or item must be forwarded to the HSRO. If the study or item is approved by CIRB, the HSRO shall be so notified by the CIRB and the information from CIRB and the HSRO shall be processed for facilitated UM IRB review as required.

Amendments to an approved study need not be reviewed by the UM IRB. Following CIRB approval of a study, continuing report or final report, however, facilitated UM IRB review shall be conducted by the UM IRB chair or designees. A goal of this review is to determine whether there are local concerns that need to be addressed and whether to accept the CIRB review as constituting approval by the UM IRB. This requires that the UM reviewer examine the submitted study materials including the protocol and informed consent documents to confirm that they are appropriate to the local context.

The UM reviewer may make the following determinations:

1) Accept the CIRB review without modifications
2) Accept the CIRB review "with modification to the protocol and/or consent form". Although no CIRB approved information may be deleted from the consent document, the UM reviewer may make minor word substitutions or additions to facilitate local comprehension and make also add information on additional risks.
3) Not accept the CIRB review. This shall occur if the reviewer believes that revisions/changes to the protocol or consent documents are more than those described above and require full board review at the local level. Once a CIRB review is deferred to the UM IRB, the CIRB shall not serve as the serve as the IRB of record for the study at the UM site.

If the CIRB review is accepted, CIRB will become the IRB of record for the protocol. CIRB will review amendments, non-local SAEs, and continuing reports for this study and will take all necessary actions. These reviews will be posted on the CIRB website. If the CIRB review is deferred to UM IRB, the UM IRB rather than CIRB will be the IRB of record for this study. The UM IRB shall be responsible for review of local SAE’s and for oversight of local conduct of the study.
SECTION 20: POLICIES SPECIFIC TO CERTAIN TYPES OF RESEARCH
20.1 MEDICAL CASE REPORTS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: February 22, 2007

A common question is whether a "medical case report" is considered human subject research and thereby requires prospective IRB review. For this purpose, a medical case report must fit all of the following criteria:

1) It is a description of medical observations or an interesting medical condition, innovative treatment, presentation, disease progression or outcome
2) It relates to three or fewer patients
3) The patients must be those treated by the clinician preparing the report
4) The report describes observations and is not presented as a systematic investigation designed to contribute to generalizable knowledge
5) The report usually contains no data analysis or testing of a hypothesis

Medical case reports that fit the above criteria do not meet the federal definition of human subject research since the information in the case report is not considered generalizable knowledge. Therefore, clinicians at the University are not required to obtain IRB approval for case reports of 1-3 patients. The review of medical records for publication in such case reports, however, is subject to HIPAA rules and may require authorization from the patient to use the protected health information.

When it is expected that observations will be made from a larger series of patients (more than three), it is usual that data will be systematically collected to answer a specific research question. Such activity is considered research and the proposed study must be submitted to the IRB for review and approval prior to its commencement.

Investigators are cautioned to distinguish between the use of innovative treatments in their clinical practice and treating patients with intent to acquire data in a systematic manner for research purposes and to contribute to generalizable knowledge.
20.2 RETROSPECTIVE CHART REVIEWS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: June 5, 2007

20.2(a) GENERAL PRINCIPLES
"Retrospective Chart Reviews" of existing medical records that are intended as a systematic investigation designed to contribute to generalizable knowledge require prior IRB approval.

For this definition, "medical records" consist of information collected and generated for the purpose of providing health care for the personal benefit of the patient. It is usual that the information within medical records will have clinical validity and utility and that the collector of the information is a health care provider.

Medical records are distinguished from "research records" since the latter are collected and generated for the purpose of providing information about a research question. The intent in collecting research records is to conduct research and the collector of the information is a researcher.

Retrospective chart reviews of existing medical records do not require prospective IRB approval if any of the following intentions apply:
1) The intent is a non-generalizable investigative review such as for quality assurance or a review of a physician's competency
2) The intent is for quality management issues such as to ascertain the need for health care delivery
3) The intent is for compliance issues such as those of third party billing or investigator non-compliance
4) The intent is to obtain clinical information for teaching purposes.

If the intent of a retrospective review of medical charts does not fit those defined above, the retrospective chart review should be considered research and must receive prospective IRB approval.
20.2(B) APPROVAL CATEGORIES FOR RETROSPECTIVE CHART REVIEWS

No matter the review category, waivers of informed consent and HIPAA regulations may be requested. Such requests must be appropriately justified in writing.

1) EXEMPT REVIEW:
A retrospective chart review may receive IRB approval under the exempt process if the research fits both of the exempt criteria of 45 CFR 46.101(b)(4). These exempt criteria are:

a. The research involves the collection or study of existing data, documents, records, pathological specimens or diagnostic specimens; AND

b. The data sources are publicly available or the data is recorded by the investigator in an anonymous manner such that subjects cannot be identified directly or through identifiers linked to the subject

2) EXPEDITED REVIEW:
Retrospective chart reviews may qualify for expedited review according to 45 CFR 46.110 category 5 if:

a. The research involves no more than minimal risk or minor changes in approved research; AND

b. The research involves materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as for medical treatment or diagnosis).

The expedited review procedure may not be used for studies in which identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' 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.

Unlike exempt review, expedited review of retrospective charts does not require that the data be de-identified or anonymous. Expedited reviews can be given to studies in which the data already exists, but data may be prospectively collected. No matter whether the data exists or will be prospectively collected, the HIPAA "minimum necessary" rule applies.

3) FULL BOARD REVIEW:
Retrospective medical chart review studies that do not meet the criteria outlined in categories 1 and 2 must be approved by a convened meeting of the full IRB panel. Examples of such studies might be those in which the information contained in the medical records is of a sufficiently sensitive nature that additional safeguards are necessary to protect subjects' rights. In this case, the full IRB panel will make a determination of risk and the need for informed consent.
20.3 Off-Label Use of Marketed Drugs, Biologics or Medical Devices

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: February 22, 2007

Questions often arise as to whether the "off-label" use of marketed drugs, biologics and medical devices constitutes research which requires IRB approval.

Physicians may sometimes use legally available drugs, biologics or devices for other than their FDA-approved indications when they determine that such "off-label" use is in the best interests of the patient. "Off-label" use should be consistent with good medical practice and the best interests of the patients and should be based on firm scientific rationale and sound medical evidence. Physicians should be well informed about the product and maintain records of the product's use and effects.

It is sometimes difficult to determine whether "off-label" use of drugs, biologics or devices is for therapeutic or research purposes or both because there is often little evidence of the safety and efficacy of the drugs, biologics or medical devices for the proposed use. The key to determining whether the "off-label" use is therapeutic or research is the physician's intent. If the intent is investigational (i.e. the seeking of generalizable knowledge of the drug, biologic or device's safety or efficacy or if the "off-label" use is intended to prove or disprove a hypothesis or to answer a question, then the use should be considered research requiring the submission of an IND (Investigational New Drug Application) or IDE (Investigational Device Exemption) from the FDA (unless the FDA specifies in writing that an IND or IDE is not required) and IRB approval for the study [c.f. 21 CFR 312.3(b)].

Submission of an IND or IDE and IRB review/approval are not required when the 'off-label' use of a marketed drug, biologic or device is not intended for research but rather is intended only for the practice of medicine or when all of the following six conditions for the "off-label" use are met [21 CFR 312.2(b)(1)]:
1) It is not intended to be reported to the FDA in support of a new indication for use or to support any other significant change in the labeling for the drug
2) It is not intended to support a significant change in the advertising for the product
3) It does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product
4) It is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively]
5) It is conducted in compliance with the requirements concerning the promotion and sale of drugs [21 CFR 312.7]

6) It does not intend to invoke 21 CFR 50.24 which is the regulation on waiving informed consent requirements for emergency research [NOTE – Regulations on the permissible, one-time emergency use of a test article with notification to the IRB within 5 days are 21 CFR 56.102(d) and 21 CFR 56.104(c)]
20.4 DATABASES, REGISTRIES AND REPOSITORIES

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: June 11, 2007

20.4(A) GENERAL PRINCIPLES
Policies in this section apply to the collection/submission, storage and use over time of information and/or biological specimens in databases, registries and repositories.

[NOTE -- Databases, registries and repositories are all considered “repositories” for regulatory purposes. Any reference in this policy to repositories applies equally to databases and registries.]

Repositories may be created for research purposes, diagnosis or clinical purposes or for both. No matter how created, repositories may receive data or specimens from multiple sources and may provide such data or specimens to multiple research studies.

Repositories constitute a valuable resource to research since investigators often draw upon these to address questions extending far beyond those envisioned when the repositories were first created.

The following are definitions used in these policies:

1) **Databases** – these are collections of information elements (i.e., data) arranged for ease and speed of search and retrieval. Databases may be maintained electronically or may be paper record systems. Examples of databases include:
   a. A set of observations (i.e., data) from a research study
   b. An electronic file of a medical provider’s patients
   c. A collection of diagnosis, treatment, and follow-up information from a subsection of a hospital’s patients
   d. A file of outcomes information compiled for quality assurance activities
   e. A list of potential research subjects

2) **Registries (Data Banks)** - these are collections of information elements or databases whose organizers:
   a. Receive information from multiple sources
   b. Maintain the information over time
   c. Control access to and use of the information by multiple individuals and/or for multiple purposes, which may evolve over time
Registries often contain codes that link information and specimens to their donor’s identify. Examples of well-known registries and data banks include:

a. Centers for Disease Control & Prevention (CDC) State Cancer Registries
b. National Registry of Myocardial Infarction (NRMI)
c. The National Practitioner Data Bank
d. The US Census 2000 Data Bank

3) **Repositories (Tissue Banks)** - these collect, store and distribute human tissue materials for research purposes.

Repositories usually include demographic and/or medical information about specimen donors and often maintain codes that link the information and specimens to their donor’s identity.

Examples of well-known repositories include:

a. The National Human Radiobiology Tissue Repository
b. The National Institute on Aging (NIA) Cell Repository
c. The National Marrow Donor Program (NMDP) Research and Outcomes Repositories

4) **Repository Principal Investigator** – a researcher with primary responsibility for the storage and distribution of the data or specimens in a repository and who, by virtue of this responsibility, has access to private health information in the repository. The repository principal investigator is responsible for maintaining a consent form and authorization corresponding to every new subject enrolled (unless waivers are granted by the UM IRB) [**NOTE – Some institutions use the term "repository manager"]

5) **Collection (or Submission) Principal Investigator** – a researcher with primary responsibility for the collection (submission) of data or specimens to the repository [**NOTE – An individual may be a repository principal investigator and also serve as principal investigator of a collection protocol”**]

6) **Submitting Investigator** – a researcher approved by the IRB to provide data or specimens to an IRB-approved repository

7) **Recipient-Investigator** – a researcher who wishes to use for research purposes data or specimens that are stored in the repository

It is usual that recipient-investigators will not be provided access to the identities of donors or to information through which the identities of donors may readily be ascertained. When no identities are available, the study being conducted by the recipient-investigator should be submitted for IRB review and may be exempt from the federal regulations governing human subject research. If recipient-investigators wish to receive identifiable, private information, however, they are considered to be 'engaged' in human subject research. This requires that their study receive prior review and approval (and continuing oversight) by the IRB and that they obtain an Assurance of Compliance.
The use of databases, registries and repositories in research is governed by both the federal human subject protection regulations at 45 CFR 46, 21 CFR 50, 21 CFR 56, 21 CFR 812, the federal privacy rule regulations at 45 CFR 160 and 164 and by the UM IRB Policies and Procedures. These regulations (and additional guidance available on the OHRP website at http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm) define that separate IRB review and approval and continuing IRB oversight must be given to:

1) The collection of data or specimens; i.e. the collection protocol [NOTE – One or more collection protocols may be submitted]
2) The operation of the repository as a storage and data management center; i.e. the repository protocol
3) The use of data or specimens in research; i.e. the research protocol [NOTE – individual research protocols must be submitted to the IRB for each research study that proposes to use data or specimens from the repository]

The requirement for IRB approval of collection, repository and research protocols applies regardless of whether the repository was initially created for research or clinical purposes.

20.4(B) IRB OVERSIGHT OF DATABASES, REGISTRIES OR REPOSITORIES
The responsibility of the IRB varies with the intent and use of a repository. Situations include:

1) **IRB approval and oversight is not required** for repositories created, maintained and operated for purposes that are totally unrelated to research. Such purposes may include diagnosis, treatment, billing marketing, quality control and public health surveillance.
2) **Prospective IRB approval and continuing IRB oversight is required** for repositories established, maintained and operated for present or future research purposes [NOTE – The principal investigator(s) responsible for data/specimen collection and for the operation of the repository must each submit an application (the collection protocol(s) and the repository protocol respectively) to the IRB for approval]
3) **Prospective IRB approval and continuing IRB oversight is required** for each non-exempt study using collected items from the repository [NOTE – Prospective IRB approval of a research protocol and continuing IRB oversight is required for studies using data or specimens from repository even if this repository was created for purposes unrelated to research]

20.4(C) THE “COLLECTION” PROTOCOL
Establishment of a repository requires that one or more 'collection protocols' be submitted by one or more collection principal investigators to the IRB for prospective review and approval. Responsibilities of the collection principal investigator include ensuring that he/she and other data/specimen submitting investigators are in compliance with regulations, UM policies and the collection and repository protocols.
Written Policies and Procedures for the Protection of Human Subjects in Research

Unless appropriately waived by the IRB, a key responsibility of data/specimen collection is the obtaining of informed consent from each donor-subject in accordance with regulations at 45 CFR 46.116 and 21 CFR 50 SubPart B. Informed consent is required since standard treatment and surgical consents rarely meet the regulatory standards for research informed consent.

Since repositories with linked or identifiable samples may be used by multiple researchers and/or for multiple purposes which may evolve over time, all of the usual elements of consent and HIPAA authorization apply and the consent/authorization process should clearly inform subjects about:

1) The general concept and purpose of repositories
2) The name and purpose of the specific repository for which consent is being solicited
3) The operation of the repository
4) As specifically as possible, the types of research that the repository will support
5) The conditions and requirements under which data and/or specimens will be shared with recipient investigators
6) The repository's physical and procedural mechanisms for protecting subjects' privacy and maintaining the confidentiality of data/specimens
7) Specific risks related to any potential breach of confidentiality related to the items being collected
8) When human genetic research is anticipated, information should include possible consequences of genetic testing (e.g., insurance risks, paternity determinations) and related confidentiality risks
9) Where applicable, the fact that the specimens may be used for future research that is not yet identified and/or that the specimens may be shared with other institutions or transferred to other institutions

[NOTE – Informed consent documents may not include any exculpatory language through which subjects are made to waive or appear to waive any legal rights]

The data/specimen collection process should also include:

1) Informing donor/subjects on whether subsequent investigators will contact them and what types of information they (the donor/subjects) can expect to be given
2) Offering donor/subjects the choice of refusing re-contact unless ethical considerations require re-contact
3) Providing donor/subjects with a means to withdraw consent for use of his/her information or specimens at any time
4) Seeking specific consent from donor/subjects for research results to become part of their medical records
5) Indicating in consent documents that researchers may refer back to the donor/subject's medical record.
Collection of data or specimens by institutions other than UM, JHS or affiliates for a UM and/or JHS repository requires approval by the IRB convened by the collecting institutions under its FWA. This is because the local IRB is familiar with the particular circumstances of its research setting and is in the best position to weigh local standards, institutional policies and resources and the needs of differing subject populations.

The “collection protocol” should also include a written submittal agreement for tissue collections. This is an acknowledgement that that the collecting investigators shall be compliant with regulations, UM policies and the provisions of the approved collection and repository protocols. The submittal agreement should also inform collecting investigators that they are prohibited from providing recipient-investigators with access to the identities of donor-subjects or to information through which the identities of donor-subjects may readily be ascertained.

20.4(D) THE “REPOSITORY” PROTOCOL
The operation of the repository and its policy/procedure for the acceptance, storage and sharing of collected items from a research repository must be approved by

1) The IRB responsible for the review, approval, and oversight of the repository; and
2) The IRB responsible for research at the site where the collected items are used.

The UM IRB is responsible for research repositories maintained at/by UM, JHS or affiliates. This requires UM IRB approval of a repository protocol which must include informed consent documents, HIPAA authorizations and information on how collected items from these repositories may be accessed, used, shared.

If collected items from a UM or JHS repository are provided to recipient-investigators outside UM and its affiliates, use and disclosure of the collected items must also comply with any additional requirements of the recipient institution and its IRB.

If the research repository is outside of UM or JHS or their affiliates, use and disclosure of collected items for UM/JHS studies must comply with any conditions stipulated by the sending institution’s IRB. The UM/JHS studies must receive prior review and approval and continuing oversight by the UM IRB and all UM policies and procedures for the protection of human subjects and the use and disclosure of protected health information must be observed.
Applications to the IRB to establish and operate a repository for research purposes (i.e. the 'repository protocol') should include at least the following information:

1) Types of data or specimens to be collected in the repository
2) The specific conditions under which items may be accepted into the repository, including submission to the repository of a copy of each subject’s signed authorization and signed consent document
3) Process for 'depositing' data or specimens into the repository including what data is stored with the
4) A detailed description of the physical and procedural mechanisms for the secure receipt, storage, and transmission of information and specimens ensuring adequate provisions are in place to protect subjects' privacy and maintain the confidentiality of subjects’ items
5) The specific conditions under which data and/or specimens may be shared with or released to recipient investigators
6) The process by which recipient investigators may request data or specimens which includes the requirement that recipient studies have prior IRB approval
7) Who is responsible for ensuring that any requests for sharing made to the repository are fulfilled and that they meet the repository's specifications
8) If applicable, the process for dealing with 'retrospective' samples' (i.e. those collected under different studies
9) What will the data include (i.e. identifiers, etc)
10) Who will have access to information in the repository
11) How long will data or specimens be maintained
12) Will subjects have a way to withdraw their submitted data or specimens
13) A sample informed consent document containing the elements of consent defined in the UM ‘Collection Protocol’ policy (above)

It is recommended that a Certificate of Confidentiality be obtained to protect confidentiality of the repository specimens and data.

20.4(E) RESEARCH PROTOCOL(S)
A research protocol must be submitted and approved by the IRB for the initiation and continuance of any study using specimens from the repository unless the repository from which the tissue/data is being obtained has an approved protocol for releasing tissue/data that is de-identified or includes only a code or otherwise is considered a limited data set under HIPAA. Recipient investigators seeking access from the repository to tissue/data that is de-identified, coded or a limited data set may be required to sign a usage or data use agreement with the University.
It is recognized that obtaining informed consent by recipient investigators, especially from non-research databases, registries and repositories, may be problematic. The latter is because the research use was not anticipated at the time of collection so that research informed consent was not usually obtained from the individuals who provided the information or specimens. In such situations, the recipient investigator may request (with written justification) that the IRB waive (or alter) the usual informed consent requirements. The IRB may approve this waiver if it finds and documents, per HHS regulations at 45 CFR 46.116(d), that:

1) The research involves no more than minimal risk to the subjects; AND
2) The waiver (or alteration) will not adversely affect subjects’ rights and welfare; AND
3) The research could not practicably be carried out without the waiver; AND
4) When appropriate, the subjects will be provided with additional pertinent information after participation [NOTE – This last criterion rarely applies to research involving information or specimens from databases or registries]

Research protocols should include a written usage agreement for signature by the research principal investigator. This acknowledges that the research principal investigator shall be compliant with regulations, UM policies and the provisions of the approved repository protocol. The usage agreement should also require recipient investigators to report promptly to the repository and to the HSRO any proposed changes in the research project and any unanticipated problems/events involving risks to subjects or others and also that data or specimens from the repository may only be utilized in accordance with the conditions stipulated by the UM IRB. Any additional use of this material requires prior review and approval by the UM IRB and, where appropriate, by an IRB at the recipient site, which must be convened under the applicable OHRP FWA.

20.4(F) PRIVACY (HIPAA) POLICIES FOR THE RESEARCH USE OF ITEMS FROM REPOSITORIES APPROVED

Under the HIPAA privacy rule, protected health information (PHI, i.e., identifiable health information) in research or non-research repositories held at the University of Miami or JHS or their affiliates covered by HIPAA may not be used or disclosed for research except as allowed in the UM and/or JHS HIPAA: Research and Patient Privacy Policy. Such use or disclosure of PHI for research requires:

1) Obtaining written authorization from the patient-subject; OR
2) IRB approval and documentation of a formal waiver of the authorization requirement; OR
3) The holder of the PHI receives and documents the HIPAA required representations from the investigator and determines that the research involves only one or more of the following:
   a. Decedents’ information
   b. De-identified information
   c. Limited data sets
   d. Review preparatory to research.
If research use was not anticipated at the time of collection, authorization for research may not have been obtained from the individuals who provided the information or specimens to the non-research database or repository. In such situations, an alternative mechanism for accessing the relevant PHI is required.

**Waiver of Authorization**

The most flexible mechanism for obtaining existing PHI for research without authorization is through a waiver, which the IRB may approve if it finds and documents, per HHS regulations at 45 CFR 164.512(i)(2)(ii) that:

1) The use or disclosure of PHI involves no more that minimal risk to the privacy of individuals based on (at least) ALL of the following:
   a. An adequate plan to protect the identifiers from improper use and disclosure; **AND**
   b. An adequate plan to destroy the identifiers at the earliest possible opportunity unless there is a research or a health justification for retaining them (or retention is required by law); **AND**
   c. Adequate written assurances that the PHI will not be reused or disclosed to another person or entity (except as required by law, for authorized oversight of the research, etc.)

2) The research could not practicably be conducted without the alteration or waiver

3) The research could not practicably be conducted without access to and use of the PHI

Investigators who believe that criteria (1) and (2) and (3) apply to their research may request for waiver of authorization on the IRB application.

**Alternatives to Authorization Waivers**

1) **Decedents' Information:**
   Investigators whose research solely involves information about deceased individuals may submit HIPAA required representations on the UM HIPAA form (Form D) to the holder of the PHI (i.e., UM, JHS etc.). Because human subject regulations do not apply to deceased individuals, an IRB application is not required.

2) **De-identified Information:**
   Investigators whose research solely involves de-identified information may indicate that at the appropriate section of the IRB application, whether for exempt, expedited or regular IRB review.

3) **Limited Data Sets and Reviews Preparatory to Research:**
   For studies involving only limited personal identifiers or for reviews preparatory to research, investigators may utilize a data-use agreement with the covered entity and/or repository to obtain the collected items. It is usual; however, that such restricted information is not sufficient for most studies.
20.5 General Principles of Informed Consent

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: April 15, 2013

Clinical investigations of devices are subject to the Investigational Device Exemptions (IDE) regulations, 21 CFR 812.

An approved IDE permits a device that is not approved (via premarket authorization, PMA) or cleared for marketing (via 510(k)) by the FDA to be shipped to conduct clinical investigations of that device. Significant risk investigational devices must have an IDE issued by FDA before they can be shipped. If an investigational device does not have an Investigational Device Exemption (IDE) number, the IRB must categorize the device as either “significant risk” or “non-significant risk.”

Under 21 CFR 812.3(m), a significant risk device means 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 use 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 device is one that does not meet the definition for a significant risk device. A nonsignificant risk device study requires only IRB approval prior to initiation of a clinical study. Sponsors of studies involving non-significant risk devices are not required to submit an IDE application to FDA for approval. Submissions for nonsignificant device investigations are made directly to the IRB of each participating institution. Sponsors should present an explanation to the IRB where the study will occur of why the device does not pose a significant risk. If the IRB disagrees and determines that the device poses a significant risk, the sponsor must report this finding to FDA within five working days [§812.150(b)(9)]. FDA considers an investigation of a nonsignificant risk device to have an approved IDE when IRB concurs with the nonsignificant risk determination and approves the study.
When research is conducted to determine the safety or effectiveness of a non-significant risk device, the institution confirms that the device fulfills the requirements for an abbreviated IDE (21 CFR 812.2(b)(91):

- The device is not a banned device;
- The sponsor labels the device in accordance with 21 CFR 812.5
- The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;
- The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator’s care, consent under 21 CFR 50 and documents it, unless documentation is waived;
- The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations;
- The sponsor maintains the records required under 21 CFR 812.140(b)(4) and (5) and makes the reports required under 21 CFR 812.150(b)(1) through (3) and (5) through (10);
- The sponsor ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 21 CFR 812.150(a)(1), (2), (5) and (7); and
- The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.

The risk determination should be based on the proposed use of a device in an investigation, and not on the device alone. For a device study to be eligible for expedited review, it must involve a non-significant risk device and the research must present no greater than minimal risk to the subject (21 CFR 56.110). If the IRB makes an initial determination that a device under study is non-significant risk and that the study is “minimal risk,” the convened IRB may vote to expedite the study at the time of continuing review assuming no change in risk level in the interim.

If the IRB decides the device is of “significant risk,” the investigator must be notified of the decision, the investigator must notify the sponsor to obtain an IDE number, or, if there is no sponsor, the investigator must contact the FDA to obtain an IDE number or a letter from the FDA stating that an IDE for that device is not required. Clinical investigations that are exempt from IDE regulations still require IRB review and approval. An investigation of a medical device in human subjects research that is exempt from the IDE regulations must fall into one of the following categories (criteria in 21 CFR 812.2(c)):

- A device legally marketed in the US that is used or investigated in accordance with the indications in the FDA-approved labeling.
- A diagnostic device (that is, an in vitro diagnostic device) if the testing:
  - Is noninvasive
  - Does not require an invasive sampling procedure that presents significant risk,
• Does not by design or intention introduce energy into a subject, and
• Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
• A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.
• A custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.
• A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.
• A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.

In vitro diagnostic (IVD) device investigations may be exempt from the IDE requirements of 21 CFR 812 if the devices are properly labeled and meet the criteria set forth in 21 CFR 812.2(c)(3). However, such studies are still subject to the FDA regulations and IRB review requirements if the research is to support an application for research or marketing of the device (see 21 CFR 50.1). This is true regardless of whether the samples to be used are individually identifiable or not. The FDA regulations define a subject to include a human on whose specimens an investigational device is used (21 CFR 812.3(p)). Thus, an IVD study to support a premarket submission to the FDA is considered a human subject investigation and is subject to IRB review under 21 CFR 50 and 56. IVD research may be eligible for expedited review and without informed consent if the study involves leftover human specimens and as long as subject privacy is protected by using only specimens that are not individually identifiable, when appropriate.

In addition to the above, FDA Guidance on informed consent for in Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable makes clear that IRB review is one of several criteria for IVD studies using leftover specimens that are not individually identifiable.

On September 8, 1995, FDA entered into an agreement with the administrator of the Medicare program, the Health Care Finance Administration (HCFA), to provide information about devices under an IDE to aid in its reimbursement decisions. [Please note that HCFA is now known as the Centers for Medicare & Medicaid Services (CMS).] Under this agreement certain devices could be viewed as “reasonable and necessary” by Medicare and treatments could be covered if
all other applicable Medicare coverage requirements are met. Specifically, FDA will place all
IDEs it approves in one of two categories:

**Category A - Experimental**

The IDE involves innovative devices in which “absolute risk” has not been established (i.e.,
initial questions of safety and effectiveness have not been resolved and thus FDA is unsure
whether the device type can be safe and effective)

**Category B - Investigational; Non-experimental**

The clinical investigation involves device types believed to be in classes I or II or device types
believed to be in class III where the incremental risk is the primary risk in question.

Class I medical devices present minimal potential for harm to the user and are often simpler in
design than Class II or Class III devices. These devices are subject only to general controls
which cover such issues as manufacturer registration with the FDA, good manufacturing
techniques, proper branding and labeling, notification of the FDA before marketing the device,
and general reporting procedures. Devices in this category include tongue depressors, bedpans
and other similar types of common equipment.

Class II medical devices are those for which general controls alone are insufficient to assure
safety and effectiveness, and additional existing methods are available to provide such
assurances. Therefore, Class II devices are also subject to special controls in addition to the
general controls. Special controls may include special labeling requirements, mandatory
performance standards, and post market surveillance. Class II medical devices are held to a
higher level of assurance than Class I medical devices in that they will perform as indicated and
will not cause injury or harm to patient or user. Devices in this class are typically non-invasive
and include x-ray machines, PACS, powered wheelchairs, infusion pumps, surgical drapes,
surgical needles and suture material.

Class III devices are those that support or sustain human life, are of substantial importance in
preventing impairment of human health, or which present a potential, unreasonable risk of
illness or injury. Due to the level of risk associated with Class III devices, FDA has determined
that general and special controls alone are insufficient to assure the safety and effectiveness of
class III devices. Therefore, these devices require a premarket approval (PMA) application
under section 515 of the FD&C Act in order to obtain marketing clearance.
The IRB will include the following statement in the informed consent document for applicable IDE Category B device studies as indicated in written communication from the FDA documenting the IDE number and the category B device designation:

“You or your insurance company will be billed only what the University will pay to obtain the device from the manufacturer.”
SECTION 21: INFORMED CONSENT
21.1 General Principles of Informed Consent

Review Responsibility: IRB Policy and Procedure Committee  
Current Approval Date: June 6, 2007

Informed consent is a fundamental and thoughtful process to ensure respect for human subjects and to ensure that their initial and continuing participation in studies is an informed, voluntary act. With few exceptions, no study may involve a human participant unless the human participant is fully informed of the basic elements of the study and the Principal Investigator has obtained the legally effective, informed voluntary consent of the subject or the subject's legally authorized representative PRIOR to the subject's participation. Appropriate documentation of the informed consent process is required unless that documentation has been waived by the IRB. The informed consent document should be signed and dated by the subject or his/her legally authorized representative and by the person obtaining consent and/or a witness who attests with his/her signature to the appropriateness of the consent process. The Principal Investigator is responsible to ensure that the requirements of informed consent are fulfilled.

The person who obtains consent from the subject must be the Principal Investigator or an individual designed by the PI to perform this function. The IRB shall require that the Principal Investigator submit to the IRB, on application and/or amendment forms, the names of all individuals who, in addition to the Principal Investigator, will be authorized to obtain informed consent from the subjects in the study. All of these individuals must have adequate knowledge about the study to be able to answer questions posed by the subject. These individuals must also have completed training including CITI certification. The Principal Investigator must obtain IRB approval prior to adding additional individuals to the authorized list. All consent forms must include a line on which the individual(s) who obtained informed consent is (are) identified by name(s), signature(s), and date(s).

For most research, no separate (i.e. third party) witness signature on the consent documents is required. Rather, the role of the witness may be satisfied by the person obtaining consent. However, there are circumstances where federal regulations, study sponsors and/or the IRB may require that a third party (a witness) be part of the informed consent process and sign the consent form. Examples of such instances include when the risks of the research are greater than minimal, where there is a potential for coercion or where the subject has limited mental capacity.

Should a subject be incapable of reading and understanding the consent process, there must be a witness present during the entire consent process who must attest to the accuracy of the presentation and the apparent understanding of the subject. This witness should sign and date the consent documents in addition to the person obtaining consent and the procedures pursuant to the utilization of a short-form written consent (c.f. Policy 21.5) should be followed.
Other key principles of informed consent include:

1) **Use Understandable Terms:** Procedures used to obtain informed consent should be designed to educate subjects and/or their representatives in understandable terms. Except as provided below, the procedures used to obtain informed consent should describe the study's purpose, the duration of the subject's participation, a description of the procedures, reasonably foreseeable risks, and benefits that may reasonably be expected from participation.

Informed consent documents should explain that participation in the research study is voluntary and will not result in any penalty if the participation is withdrawn or not given. This information should be written and communicated in a manner that is understandable to the people being asked to participate. Every effort should be made to express a scientific concept/idea in lay terms at an approximate 6th grade reading and comprehension level. A copy of the signed consent form shall be given to the subject.

2) **Sufficient Time for Careful Decision-Making:** Investigators should seek consent from potential or current subjects only under circumstances that provide the subjects and/or their representatives with sufficient time to read the consent form, to question and discuss the information and to carefully decide whether or not to volunteer for the study. Language in the informed consent documents and process should not be coercive.

3) **Thorough Information:** During the informed consent process, subjects should be sufficiently informed about the research study including its procedure, risks and anticipated benefits, and alternative procedures (where therapy is involved). Federal regulations define eight required elements of informed consent that must be included in this documentation in compliance with 45 CFR 46.116 and 21 CFR 50 SubPart B. These are defined more completely in Policy 21.3 on "Required Elements of Informed Consent".

In addition to the eight "required elements of consent", federal regulations at 45 CFR 46.116(b) and 21 CFR 50.25 define six additional elements of informed consent which, based on their individual appropriateness, shall be provided to each subject. These are also included in Policy 21.3 *(below)*.

*[NOTE – Guidance on writing informed consent documents with UM-required language that applies to certain situations is included on the HSRO web-site at www.hsro.miami.edu.]*

4) **Questions and Comments:** Subjects should be offered the opportunity to ask questions and to withdraw at any time from the research. They should also be informed about how subjects are selected, the person(s) responsible for the research and the mechanism(s) by which their comments and/or complaints will be received and acted upon. To ensure that this principle is met, an appropriate (IRB approved) individual should be present or available when the consent form is reviewed by a prospective subject and/or his/her representative, to be certain that the consent form is fully understood and that any questions are answered.
5) **No Exculpatory Language:** Informed consents, no matter whether oral or written, should not include any exculpatory language through which subjects or their representatives are made to waive or appear to waive any of the subject's legal rights, or that releases or appears to release the Principal Investigator, the sponsor, the institution or its agents from liability for negligence.

6) **Minimize Coercion or Undue Influence:** Informed consents, no matter whether oral or written, should be communicated in a manner that minimizes the possibility of coercion or undue influence directed toward subjects and/or their representatives.

7) **Voluntary Participation:** Informed consents should define that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subjects is otherwise entitled, and that the subjects may discontinue participation at any time without penalty or loss of benefits to which the subjects is otherwise entitled.

Principal Investigators shall submit to the HSRO for IRB review revisions of consent documents when changes are appropriate due, for example, to new information or to improve the consent process. If significant revisions are approved by the IRB, the PI and/or the IRB shall require that currently enrolled subjects sign the new consent form.

Principal Investigators should make provisions so that an IRB-approved individual is available who can communicate with the research subject during the consent process and over the course of the study (during both working and non-working hours).
21.2 WAIERS OR MODIFICATIONS OF INFORMED CONSENT

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: July 13, 2006

The requirement for informed consent applies to all active studies unless the IRB grants a waiver of this requirement. IRB approval of studies as "exempt" does not necessarily mean that the research is exempted from the informed consent requirements.

In response to a request from the Principal Investigator and based on specific criteria (see below), the IRB may waive the requirement to obtain informed consent for some or all participants or it may approve a consent procedure which does not include, or which alters, some or all of the required elements of informed consent [NOTE – These elements are defined in 45 CFR 46.116(c) – c.f. Policy 21.3]. For research involving an FDA-regulated product, however, the IRB may only waive the requirement for informed consent in emergency situations.

For research that does not involve an FDA-regulated product, an IRB decision to waive or modify informed consent may be made on an expedited basis by the IRB Chair or designee during his/her expedited review of the study or amendments or by the convened IRB. The decision as to whether expedited or convened IRB review is necessary shall be made pursuant to regulations and policies on expedited or convened IRB reviews [c.f. Section 8].

An IRB decision to waive or modify informed consent requires that the IRB find and document that:
1) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
   a. Public benefit or service programs; OR
   b. Procedures for obtaining benefits or services under those programs; OR
   c. Possible changes in or alterations to those programs or procedures; OR
   d. Possible changes in methods or levels of payments for benefits or services under those programs; AND
2) The research could not practically be carried out without the waiver or alteration

The IRB may also approve a consent procedure which does not include, or which alters some or all of the required elements of informed consent described in 45 CFR 46116(d)), or the IRB may waive the requirements to obtained informed consent, if the IRB finds and documents that:
1) The research involves no more than minimal risk to the subjects; AND
2) The waiver or alteration will not adversely affect the rights and welfare of the subjects; AND
3) The research could not practicably be carried out without the wavier or alteration; AND
4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all participants (c.f. 45 CFR 46.117; 21 CFR 56.109) if it finds either that:

1) The only record linking the participant and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each participant will be asked whether the participant wants documentation linking the participant with the research, and the participant's wishes will govern (does not apply to research regulated by FDA); OR

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

The IRB shall take into account special circumstances that may warrant waiving formal written consent. For example, fieldwork and ethnographic research may involve observations and interactions with subjects in their own environment, often over long periods of time. In such situations, there may be continuing and evolving protocol shifts such that informed consent statements may never accurately reflect the evolving experimental protocol.
21.3 REQUIRED ELEMENTS OF INFORMED CONSENT

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: July 31, 2008

The IRB shall recognize that the readability, cultural sensitivity and format of informed consent documents contribute to participant comprehension and satisfaction and decrease anxiety associated with the consent process. To assure these goals, eight required elements of informed consent have been defined by federal regulations [45 CFR 46.116(a) and 21 CFR 50.25(a)]. HSRO staff may examine informed consent documents for compliance with the required elements, seek clarifications from Principal Investigators as appropriate and make recommendations to the IRB. The IRB may seek clarifications from Principal Investigators as appropriate and shall determine whether required elements of informed consent are adequately addressed during their deliberations on approval/disapproval of the documents.

The eight required elements which, unless waived by the IRB, must be included in the informed consent are:

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental
2. A description of any reasonably foreseeable risks or discomforts to the subjects
3. A description of any benefits to the subjects or to others which may reasonably be expected from the research
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subjects
5. A statement describing the extent, if any, to which confidentiality of records identify the subjects will be maintained
6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, and where further information may be obtained
7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subjects
8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subjects is otherwise entitled, and the subjects may discontinue participation at any time without penalty or loss of benefits to which the subjects is otherwise entitled
In addition to the eight required elements, federal regulations [45 CFR 46.116(b) and 21 CFR 50.25(b)] include six additional elements of informed consent. When appropriate, one or more of these elements of information shall be provided to each subject:

1. A statement that the particular treatment or procedure may involve risks to the subjects (or to the embryo or fetus, if the subjects is or may become pregnant) which are current unforeseeable
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent
3. Any additional costs to the subjects that may result from participation in the research
4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subjects
5. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject
6. The approximate number of subjects involved in the study

For studies that are subject to the requirements of the FDA regulations, consent documents and the process of obtaining consent should inform participants of the possibility that the FDA may inspect the study records including those of the participant.
21.4 Informed Consent Documents

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: April 17, 2006

When studies are approved by the IRB, the PI shall receive from the HSRO written notification together with a copy of the approved consent form containing the stamped/watermarked date of approval and the expiration date of the study's approval on each sheet. The Principal Investigator may make copies of the stamped/watermarked consent form for use in obtaining informed consent from each research subject. A copy of the stamped/watermarked approved consent form shall also be filed in the study files maintained in the HSRO. Only informed consent documents bearing the HSRO approval stamp/watermark may be used in the conduct of research.

Consent forms signed by research participants and others should be retained by the Principal investigator for a period of at least three years after the study is completed and a final report is approved by the IRB.
21.5 LANGUAGE REQUIREMENTS FOR INFORMED CONSENT

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: June 6, 2007

21.5(a) GENERAL PRINCIPLES
Individual subjects and sometimes significant portions of the subject population, may not comprehend the spoken English language or read and comprehend documents, such as those for informed consent, that are written in English. If possible, such individuals should not be excluded from research that may have potential benefits. If they are to be included, their ability to engage in the consent process and make informed decisions about participation in research and its risks and benefits must be protected. To accomplish this, informed consent documents should be presented to prospective subjects in a manner and language that they can understand. The same is true for other research related documents such as interviews or surveys.

[NOTE – The IRB may, at its discretion, approve translated versions of documents, questionnaires or other materials published in peer reviewed journals or materials previously approved by the UM IRB.]

To determine what consent documents should be used for individuals considered by investigators to be potential subject, the following policies apply:

1) If, in the view of the investigator, a potential subject can read and comprehend English at what may reasonably be considered to be at a sixth grade level or higher, the written consent form may be in English

2) If a potential subject cannot read English but can read another language, any written consent that is obtained should be in that alternative language. Any amendments or addenda to the consent form must also be in that language

3) If a potential subject cannot read English but he/she fully comprehends spoken English, the consent form may be read to the subject in English. The subject's ability to understand English should be noted in writing, and signatures of the subject, the person who obtains consent, and a witness should be obtained

4) If a potential subject cannot read either English or the available alternative language, and does not fully comprehend spoken English but does fully comprehend the alternative language when spoken, the consent form that has been translated into the alternative language should be read to the subject. The subject's ability to understand the alternative language should be noted in writing, and the signatures of the subject, the person who obtains consent, and a witness should be obtained
Written Policies and Procedures for the Protection of Human Subjects in Research

Exceptions to the above policies may be made in situations when:

1) A subject requires rapid entry into a study for his/her well-being but the study does not have a consent form fully translated in writing to the subject's language.

2) Investigators are uncertain whether non-English speaking subjects might be enrolled in a study, or believe that the majority of subjects are English speakers and that there might be only a small number of subjects (less than five) who will not understand English.

3) A waiver of written consent has been approved by the IRB. In this case, consent must be obtained verbally from all participants in whichever language was understood.

4) A waiver of consent (written and verbal) has been approved by the IRB.

In situation 1 and 2 (above), regulations [45 CFR 46.117(b)(2) and 21 CFR 50.27(b)(2)] permit the use of a short form in the subject's language together with a summary document in English. The "short form" consent document may be generic but it must affirm that the required elements of informed consent have been presented orally to the subject or the subject's legally authorized representative and that a witness fluent in both English and the subject's language was present to observe the process. When the person obtaining informed consent is assisted by a translator, the translator may serve as the witness.

The research subject or the legally authorized representative must sign only the short form. The witness must sign the short form and the IRB-approved written summary; and the person obtaining consent must sign the summary. A sample short form written document is provided on the OHRP website [NOTE —To access, click on http://www.hhs.gov/ohrp/humansubjects/guidance/ic-non-e.htm].

All foreign language versions of the complete form or the short form must be approved by the IRB in advance of their use. IRB approval of the "short form" may be by expedited review of the IRB Chair or designee, if the study and the full English language informed consent document and the English version of the short form document have already been approved by the IRB. The IRB Chair or designee may, if appropriate, defer review of the "short form" to the convened IRB.

Investigators obtaining consent within the short form process must orally present all elements of informed consent outlined in the IRB approved consent form to the subject. This presentation may be directly to the subject if the investigator speaks the same language as the subject or may be presented through an interpreter who shall convey the information to the subject. Subjects shall be given a copy of the full English consent (or summary) along with the short form in the subject's own language.

21.5(B) TRANSLATION PROCESS

If a researcher intends to enroll subjects who do not adequately read the English language, informed consent documents should be translated into a language comprehended by the potential subjects.

The English version of approved study documents, including informed consent documents, should be approved by the IRB before the documents are translated into languages other than English. This will avoid duplicate work in case modifications have to be made to the English versions before they are approved by the IRB.
Once the English documents have been approved by the IRB, the investigator may create documents in other language(s) intended for use. The translated documents must be approved by the IRB before they may be used. Documents are eligible for IRB approval if translated under the following policies:

[NOTE – Only for studies whose management has been outsourced to Western Institutional Review Board (WIRB), the applicable translation policy is that defined by WIRB]:

1) The translation may be made by a certified translator approved to conduct such business by the university. Such translations must be accompanied by a signed translator certification statement including the date of the translation. This process may be used all studies but it is required for studies involving an IDE or IND. This requirement for certified translations for FDA research involving drugs or devices is consistent with the FDA requirement that a translated document be accompanied by an "Affidavit of Accuracy".

2) The translation may be made by a "back translation" method (see below) for submission to the IRB. This process may be used for all studies that do not involve an IDE or IND.

3) The translation may be made by a qualified translator. Included in these qualifications is that the translator be fluent (i.e. can speak, read and write) in the language. The translator must attest that the translated informed consent accurately reflects the IRB-approved English informed consent and provide the date of the translation. The translator must also submit to the HSRO a signed statement describing his/her qualifications to make this translation from one specific language into another. This process may be used only for studies that are approved by the IRB as 'exempt'. [NOTE – The signed statement should define that the translation is true, accurate, and correct "to the best of my knowledge and ability".]

21.5(c) BACK-TRANSLATION PROCESS

For studies not involving an IDE or IND, a “back-translation” of IRB-approved documents is permitted. This process requires:

1) A “forward” translation from the IRB-approved English document to the target language by a translator who is fluent in both languages.

2) A “back” translation of the “forward” translation into English. This must be done by a translator fluent in both languages who is someone different from the translator who provided the “forward” translation. The back translator must create the translation independent from the “forward” translation and must attest to the fact that he/she has not seen the original English consent form.

3) Review and approval of both the forward and back translations for accuracy and completeness by the IRB.

"Forward" and "back" translations should each be made by qualified translators. Included in these qualifications is that the translators are fluent (i.e. can speak, read and write) in the target language.
The "forward" and "back" translators must each attest that the translation he/she made was done independent of the other translation, is accurate and provide the date of the translation. The "back" translator must also attest to the fact that he/she did not see or refer to the English document when making his/her translation.

Each translator must also submit to the HSRO a signed statement describing his/her qualifications to make this translation from one specific language into another. [NOTE – The signed statement should define that the translation is true, accurate, and correct "to the best of my knowledge and ability".]

The "forward" and "back" translations, the IRB-approved English documents and the information from the translators should be submitted to the HSRO for forwarding to the IRB for review and approval. The IRB Chair or designee may approve the translated documents or may refer them to the convened IRB for review and approval.
21.6 **INFORMED CONSENT AND VULNERABLE SUBJECTS**

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** April 17, 2006

Federal regulations define additional protections that must apply to certain groups of human subjects considered to be particularly vulnerable in a research setting. These include pregnant women, human fetuses and neonates, prisoners, children, cognitively impaired persons and subjects with no or limited reading ability. Included in these protections are additional requirements for informed consent documents and the informed consent process. Policies on such additional informed consent requirements are defined within the sections of these Written Policies and Procedures devoted to specific vulnerable subjects.
SECTION 22: ADVERTISEMENTS AND OTHER RECRUITMENT MATERIALS
22.1 GENERAL PRINCIPLES

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: August 6, 2008

IRB prior approval is required for all matters that are relevant to the recruitment and retention of research participants. This includes the methods and materials of recruitment, and the amounts, schedules and details of all recruitment-related payment arrangements including incentives, compensation or other inducements paid or provided to participants, investigators, organizations or to those referring research participants. After study approval, no changes may be made to recruitment methods, materials or payment arrangements unless these changes are approved by the IRB through the amendment process.

Such recruitment-related information must be fully disclosed by investigators in applications to the IRB and shall be reviewed by the IRB pursuant to policies for study or amendment approval. Applications must describe the methods by which potential subjects will be identified, contacted and recruited. Copies of all advertising or other recruitment materials or tools (with a description of how they will be used) must be submitted for IRB review and approval.

This requirement for IRB approval extends to the mode of recruitment communications and to advertisements or other recruitment materials that include (but are not limited to) tapes or other broadcast media for television, radio or internet (website) postings, advertisements, flyers, posters, brochures, newspaper advertisements, e-mail solicitations, telephone scripts, correspondence to subjects or other cooperating individuals such as referring physicians or facilities, and press releases intended to facilitate recruitment of subjects. This also includes any sponsor-provided advertisements. These materials should be submitted in their final form by the Principal Investigator to the HSRO for IRB approval with the initial application for the study; and any subsequent changes to approved materials, or any new materials, must be approved by the IRB before these changes or additions are implemented.

Internet (website) or other postings providing basic information about studies but without the intent to recruit, or without information about recruitment do not require IRB approval. Investigators may submit such materials to the IRB for its determination as to whether IRB approval is required.
Unless the IRB approves otherwise (such as for materials provided within multi-site trials), only
documents or other advertising or recruitment materials bearing the HSRO approval stamp may be
used in the conduct of research. Recruitment materials that cannot show the HSRO approval stamp,
such as e-mail solicitations, internet websites and broadcasted material must mention that the study
has been approved by the UM IRB unless the IRB approves otherwise (such as for websites managed
by external sites). Advertisements approved by the IRB must subsequently be submitted to the UM
Public Relations Office for their endorsement as to form, content, and publication method.

The requirement for IRB approval extends also to recruitment methods including screening procedures.
Such methods may include (but are not limited to):

a. **Maintaining a separate IRB-approved recruitment protocol**: this is done to develop a
database of potential participants (preparatory to research) who may be contacted by
investigators about participation in IRB-approved studies in accord with their signed consent. In
this method, IRB approval is required for participants/patients to provide consent to
subsequently be contacted for future research studies.

b. **Direct recruitment of participants unknown to investigators**: Examples include random
digit dialing, approaching people in public settings, snowball sampling and the use of social
networks.

c. **Utilizing clinical trial or other websites** to post research study information.

d. **Providing colleagues with an IRB-approved Introduction letter and/or a letter to be
distributed to individuals/patients** describing the study and contact information and asking
them to briefly inform potential participants about the study. NOTE – Potential participants may
initiate contact and/or sign an authorization to use or disclose (release) identifying health
information. Otherwise, study investigators may not have access to participant/patient
information. (This authorization must be placed in the patient’s medical record indicating
permission from the patient to be contacted for the study).

[NOTE – For such recruitment, a partial waiver of HIPAA authorization must be requested from
the IRB. This authorization does not constitute the required informed consent.]

e. **Approaching the investigator’s own patients, students, employees**. IRB review of this
method must be conducted with awareness that there may be ethical concerns if individuals
have (or are perceived to have) difficulty saying no to an authority figure. Section 23.7 of these
policies defines these individuals as potentially vulnerable and, where appropriate, provides
special protections against undue influence or coercion. Medical record review is subject to
HIPAA regulations. Additional regulations regarding student records are defined in the Family
Educational and Rights Privacy Act (FERPA).
f. **Requesting a Waiver of Consent/HIPAA Authorization, if applicable for recruitment purposes.** Waivers may be granted one or more of the following circumstances applies:

1. The study is of minimal risk and subjects will be not be contacted. In many chart review studies, for example, investigators may request and justify a complete waiver of consent/HIPAA authorization

2. A chart review is required to identify prospective subjects who will then be contacted and asked to participate in the study. In this case, investigators may request a partial HIPAA waiver with explanation why the study cannot be done without the waiver. With this partial waiver, only the minimum information needed to make contact may be collected and informed consent/HIPAA authorization must be obtained from participants before additional information is accessed.

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g. **Identifying potential participants through registries, medical records in multiple institutions or other sources.** This method, often used in large-scale epidemiological or other population-based studies, is of concern since investigators may gather health information before directly contacting potential participants. Applications for IRB approval must justify in detail why the study requires that the IRB grant a partial waiver of HIPAA authorization to obtain subjects’ identities and why the IRB should allow investigators to contact subjects directly to gather the required written informed consent and HIPAA authorization and then to proceed with information gathering and/or the research protocol.
22.2 IRB APPROVAL GUIDELINES

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: August 6, 2008

IRB review and approval requires that the privacy of potential participants is protected, that subjects are not under pressure or coercion to participate in the study and that information presented to subjects is accurate and balanced. To accomplish these goals, IRB review and approval of participant recruitment methods, advertising materials and recruitment-relevant payment arrangements shall include consideration of the study purpose and goals, the research setting(s), the special problems of vulnerable populations (c.f. policy SECTION 23) and the adequacy of safeguards to ensure that the identification and recruitment of all participants is confidential and free of coercion, undue influence or invasion of privacy. Specific criteria for IRB review and approval include:

22.2(A): RECRUITMENT METHODS AND ADVERTISING MATERIALS:
Recruitment methods and advertising materials should contain:

a. a clear statement that the activity is for research purposes
b. a simple and concise description of the purpose of the research
c. general eligibility criteria for participation
d. a brief description of the significant risks and possible benefits (if any)
e. the time or other commitments required of participants
f. contact information (including the name and address of a contact person) for use by potential participants seeking further information or to enroll
g. clear indication that the recruitment is for a “[University of Miami and/or affiliated institution] research study
h. (if applicable) a statement that the experimental drug/agent or device involved in the study is “investigation” and without FDA approval for the given indication
i. (if applicable) they should describe the possibility of receiving placebo
j. information consistent among all other study-related materials including consent forms, introductory letters to subjects, recruitment scripts and web postings

Recruitment methods and advertising materials should not:

a. be coercive or include any exculpatory language appearing to waive any potential subjects’ rights or any liability for negligence
b. imply certainty of a favorable outcome or benefit beyond what is defined in the protocol and consent forms
c. They must not be misleading or imply other benefits beyond what is indicated in the approved consent form
d. claim, either explicitly or implicitly, that:
   1. any research procedure is superior to any current practice
   2. (if applicable) any experimental drug/agent or device is known to be safe or effective
   3. (if applicable) the use of any experimental drug/agent or device is equivalent or
      superior to the use of any currently available drug/agent or device
   4. (if applicable) participants will receive “free medical treatment” when the intent is only
      that subjects will not be charged for research-related, protocol-defined treatment

e. emphasize compensation to participants or the amount of such compensation by such means
   as larger or bold type

f. For FDA-regulated research, recruitment methods and advertising materials should not:
   1. make claims, either explicitly or implicitly, about the drug, biologic or device under
      investigation that are inconsistent with FDA labeling
   2. use terms such as “new treatment”, “new medication” or “new drug” without explaining
      that the test article is investigational

An individual's decision to participate in research must be free from coercion or undue influence. The
Principal Investigator (PI) must ensure, and the IRB shall require, that all recruitment methods provide
subjects with sufficient time to consider the decision to enroll in a research study.

For initial studies, the IRB Chair or designee may provide expedited review of recruitment methods and
materials if he/she is conducting expedited review of the study. The IRB Chair or designee shall use
discretion as to whether the proposed recruitment method and/or materials fulfill the requirements
stated above and/or must be submitted to the convened IRB for review and decision. The IRB Chair or
designee may make recommendations for changes in recruitment methods or materials to the Principal
Investigator. If the IRB Chair or designee does not approve a recruitment method or materials, the
Principal Investigator may appeal to the convened IRB.

22.2(B): COMPENSATION, INCENTIVES OR OTHER INDUCEMENTS TO PARTICIPANTS:
Study participants may (but not necessarily) be compensated monetarily or provided other incentives or
inducements as symbolic recognition for their enrollment and/or continuing contributions to research.
When given, such compensation, incentives or other inducements must be limited in extent and manner
so they are not perceived to be coercive or providing undue influence or duress; and they should be
provided without regard to a subject’s economic status. Incentives, compensation and/or other
inducements to subjects should reflect the risk, discomfort or inconvenience associated with study
participation; and they should not be so large as to result in any one group of individuals (such as the
economically disadvantaged) bearing an unduly large share of the risks and burdens of research
participation.

For FDA-regulated research, compensation to subjects’ participation in a study may not include an offer
from a sponsor of a coupon good for a discount on the purchase price of the product
(drug/agent/device) once it has been approved for marketing.
Incentives, compensation or inducements must not be such that a subject’s participation in research is other than voluntary. IRB study approval requires that the promise or expectation of a reward for study participation should not influence a subject’s willingness to participate in the research. Nor should rewards influence a subject’s decision-making process such that the subject acts without due consideration of the risks of participation.

Incentives, compensation or other inducements to subjects for enrollment or continued participation in a study must be accurately explained in informed consent documents and must be fair and reasonable. This description shall include the amount and/or item and the schedule of its provision. If total compensation to a subject exceeds $600, the following IRS concept should be conveyed in the informed consent:

“The compensation you receive may be taxable. When the total compensation paid to someone participating in one or more studies is $600 or more in one calendar year, the [University or other affiliated institution paying the compensation] is required by the IRS to treat this compensation as any other payment for compensation/salary and to report the amount to the IRS. You will also be responsible for reporting this compensation when you file your tax return”

In IRB deliberations, incentives/compensation or other inducements must not be considered a “benefit” off-setting (in whole or part) “risk” to subjects. Rather, the IRB must be assured that these are not influencing subjects to participate in research that they would not otherwise choose to participate in.

Research subjects may withdraw from a study at any time and for any reason. Incentives, compensation and/or other inducements may not be provided on a schedule that may coerce or unduly influence a subject’s decision to continue participation. Incentives, compensation or inducements for the continuing participation of a subject in a study should be given on a prorated basis as the study progresses to reflect the time and inconvenience of a subject’s participation throughout a study and may not be fully withdrawn or withheld pending the subject’s completion of the study. Unless otherwise justified and IRB-approved, this proration shall be “temporal” (i.e. the amount after two study interventions and/or visits should be twice that for one study intervention/visit etc).

Additional incentives, compensation or other inducements may be provided to subjects for completing a study. Unless justified and IRB-approved, these may be no more than 10% of the fair market value of the total among all incentives, compensation or other inducements being offered to subjects at the time of their enrollment in the study.

Incentives, compensation and/or other inducements for study participation may not be provided to a group of subjects as a whole (i.e. pizza to a class of students if all participate, etc).
22.2(C): RECRUITMENT INCENTIVES/COMPENSATION, BONUSES, REFERRAL FEES OR OTHER INDUCEMENTS TO INVESTIGATORS OR TO THOSE REFERRING SUBJECTS:

Financial or other arrangements to investigators or to those referring subjects are not permitted if these could influence, or be reasonably perceived as influencing, participant recruitment or the interactions with participants. The definition of “financial or other arrangements” includes but is not limited to incentives, compensation, bonuses, referral fees or other inducements such as stock options, travel opportunities, educational stipends, merchandise, vouchers, gift certificates, medical care or other services, discount coupons, extra vacation time, academic rewards such as class credit or anything else of value.

Physicians and others including the University or affiliated institutions, clinics, laboratories, hospitals or other health care facilities or professionals may not receive “finder’s fees” for referring subjects to a research study.

Study investigators (and/or their research programs), the University or affiliated institutions may receive funds to defray the reasonable expenses of a research study. Such expenses may include (but are not limited to) the percentage of effort of personnel directly engaged in the research, costs for infrastructure, hospital fees, pharmacy charges, laboratory fees, research equipment costs, rent, recruitment advertising and compensation or incentives to subjects. If received, such expenses must be noted (on a generalized basis) in informed consent documents. Such proposed expense reimbursements must be reported by investigators to the IRB and considered for approval by the IRB based on their fair market value.

Expenses of a research study defrayed on a per-subject payment schedule should be fixed for each subject and may not increase as a result of subject enrollment meeting specific thresholds (i.e. $100 per subject for the first 10 subjects then $150 per subject for the next 10 subjects etc) unless the increase is based on a documented increase in direct expenses and approved by the IRB.
SECTION 23: VULNERABLE POPULATIONS
23.1 GENERAL PRINCIPLES

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: July 6, 2008

Federal regulations and ethical principals require that certain groups of human subjects shall be considered particularly vulnerable in a research setting. Those considered to be "vulnerable populations" are individuals who may have limited autonomy which precludes their full and free appreciation or participation in the consent process.

Particularly vulnerable populations must receive, in addition to the general requirements for review of research by the IRB, further protections which are consistent with federal regulations and specific for:
  a) pregnant women, human fetuses and neonates involved in research (45 CFR 46 Subpart B), prisoners (45 CFR 46 Subpart C), and children (45 CFR 46 Subpart D, 21 CFR 50 Subpart D). There are also additional federal regulations pertaining to “in vitro fertilization.”

Definitions applicable to these policies include:
  1. **Neonate:** a newborn
  2. **Fetus:** the product of conception from implantation until delivery
  3. **Pregnancy:** the time between implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy until the results of a pregnancy test are negative or until delivery

Although federal regulations pertain specifically to the vulnerable populations defined above, other populations, though not considered vulnerable according to regulations, may still be particularly subject to coercion. These populations, which should be considered vulnerable and deserving of special consideration by investigators and the IRB, include but are not limited to those with dementia or other cognitive impairments, students and employees of the Principal Investigator and key personnel, the elderly, terminally ill patients, hospitalized patients, prospective transplant recipients, and patients who can receive certain treatment(s) only through research protocols. Both the Principal Investigator and the IRB should recognize such subjects as vulnerable and should provide special protections as necessary.

While considering additional protections for vulnerable subjects, the IRB shall also require that members of these populations be permitted or encouraged to become human research subjects to ensure that they are adequately represented in research and have access to potential benefits of such research.
In its review of studies involving vulnerable populations, the IRB should carry out responsibilities additional to those described in other sections of these policies. For the vulnerable populations defined in Subparts B-D of 45 CFR 46 and Subpart D of 21 CFR 50, the additional responsibilities include following special procedures that ensure the safeguarding of the subjects' rights, safety and welfare. Policies associated with these specific vulnerable populations and for other populations not incorporated in the federal regulations are included in individual sections of this document (below). In general, the IRB review shall be particularly concerned with the rationale and details for the inclusion of vulnerable populations in studies, with procedures to ensure that risks are adequately addressed, with the consent process to ensure that it adequately addresses the needs and capabilities of vulnerable subjects and with the fulfilling of all necessary regulatory requirements.

To accomplish the above, the IRB membership must include one or more members qualified to represent each involved group of vulnerable subjects with knowledge, expertise and sensitivity gained from working with these subjects or from personal experience. At least one member qualified to represent the involved group of vulnerable subjects shall be present at the convened meeting when a study involving that group of vulnerable subjects is reviewed.

If the IRB believes that its expertise regarding a vulnerable population is insufficient to conduct an in-depth study review, the IRB may seek input from one or more internal or external consultants with appropriate scientific or scholarly expertise and knowledge of the vulnerable groups of subjects. The IRB has the authority to table its review until such consultant guidance/recommendation is received and presented pursuant to its policy on consultative support (SECTION 3.1).

Keys to the IRB review process for studies involving vulnerable populations include that the IRB ascertain that the inclusion of the vulnerable population is adequately justified in writing, that the Principal Investigator and the convened IRB have reviewed relevant federal regulations (45 CFR 46 Subparts B-D and/or 21 CFR 50 Subpart D) and that safeguards are implemented to minimize risks that are unique to each population. Research in vulnerable subjects shall not be performed unless all regulatory criteria are met.
23.2 IRB APPROVAL AND HHS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: April 24, 2006

For studies involving vulnerable subjects who are included in 45 CFR 46 Subparts B-D (i.e. pregnant women, human fetuses and neonates, prisoners and children) and/or 21 CFR 50 Subpart D, IRB approval may only be considered if one or more of the following conditions is met:

1) The research does not involve more than minimal risk to the subjects
2) The research is likely to benefit the subjects directly, even if the risks are considered to be more than minimal
3) The research involves greater than minimal risk with no prospect of direct benefit to individual subjects, but is likely to yield generalized knowledge about the subject's disorder or condition

If the study is approved by the IRB but it involves subjects considered vulnerable according to federal regulations in Subparts A-D of 45 CFR 46 and/or Subpart D of 21 CFR 50, and if the IRB deems that none of the above conditions is met, the study must also be submitted to the United States Secretary of Health and Human Services for review and approval.

For populations not considered with 45 CFR 46 Subparts B-D and/or 21 CFR 50 Subpart D but who are considered vulnerable by UM ethical standards and the IRB (for example, persons with dementia or other cognitive disorders, students, employees and particularly vulnerable patients), IRB review shall be guided by the principles of the three criteria listed above.
23.3 PREGNANT WOMEN, HUMAN FETUSES, AND NEONATES

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: April 24, 2006

23.3(a) PREGNANT WOMEN AND FETUSES

Federal regulations (45 CFR 46, Subpart B) and University ethical standards require that principal investigators and the IRB shall be sensitive and apply special conceptual and regulatory protections to research involving pregnant women, human fetuses and neonates (newborn children). Key among these concepts is that investigators shall acknowledge and be sensitive to the vulnerability of subjects who are pregnant or newborn especially within the unique times of labor and delivery. Investigators shall also take into account that the health and wellbeing of the mother, the fetus and/or the newborn should take priority over the goals of any research study. Investigators shall ensure the highest possible standards in the conduct of research involving pregnant patients including cooperation from all involved in the labor and delivery processes.

Pursuant to special regulatory protections and in addition to the general requirements for IRB reviews (see earlier sections of these policies), the IRB shall require, in addition to all other requirements, that the following ten conditions be met and documented to approve the involvement of pregnant women or fetuses in research (c.f. 45 CFR 46.204). These required conditions are:

1) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses; AND

2) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means; AND

3) Any risk is the least possible for achieving the objectives of the research; AND

4) If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of these policies and procedures; AND
5) If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions in these policies and procedures, except that the father’s consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest; AND

6) Each individual providing consent under conditions (4) or (5) [above] is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate; AND

7) For children [as defined in these policies and procedures] who are pregnant, assent and permission are obtained in accordance with the provisions in these policies and procedures involving children; AND

8) No inducements, monetary or otherwise, will be offered to terminate a pregnancy; AND

9) Individuals engaged in the research will have no part in any decisions as to the timing, method or procedures used to terminate a pregnancy; AND

10) Individuals engaged in the research will have no part in determining the viability of a neonate.

In conducting an IRB-approved research study involving pregnant women and fetuses, investigators should carefully and sensitively consider the process for obtaining informed consent. Whenever practical and feasible, information about the study should be made available prior to labor. If the patient must be approached during labor, permission should be sought first from the patient’s obstetric care provider and the patient’s primary nurse should be involved in discussions regarding the appropriateness of such an approach. If the obstetric care provider and/or the primary nurse believe that the patient may not comprehend a research protocol, the patient should not be approached for research participation. Investigators should also delay approaching patients for research participation if the patient’s capacity for informed consent is impaired by medications.

**Coincidental Pregnancy:** There are circumstances in which pregnancy is coincidental to participant selection within a research study. This may occur, for example, when potential participants are recruited from a population that includes women of child bearing potential. In these circumstances, the IRB shall determine such matters as whether:

1) Participants should be advised on the risks of participation in the study
2) Participants should be advised to avoid pregnancy or nursing during or following participation in the study
3) Participants should be advised to notify the principal investigator immediately should they become pregnant
4) Participants should avoid causing a pregnancy during or following participation in the study and whether the participant should notify the principal investigator should the participant cause a pregnancy
5) Pregnant women should specifically be excluded from the study or whether specified methods of contraception should be required during or following participation in the research
23.3(b) PLACENTA, DEAD FETUS OR FETAL MATERIAL
For studies involving, after delivery, any of the placenta, the dead fetus, macerated fetal material or cells, tissues or organs excised from a dead fetus, shall be conducted pursuant to federal regulations (45 CFR 46.206). The IRB may approve such research only if:
   1) The research is conducted only in accord with any applicable Federal, State or local laws and regulations regarding such activities; AND
   2) Information associated with the after delivery material described above is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent written policies and procedures herein are applicable.

23.3(c) NEONATES
As it pertains to these policies, "viable" means able, after either spontaneous or induced delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heart beat and respiration.

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of these UM written policies and procedures that pertain to general IRB reviews and to reviews of research involving children (see below). An additional condition for approving any research involving viable neonates (defined as newborns) is that the IRB shall determine and document that:
   1) Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates; AND
   2) Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate; AND
   3) Individuals engaged in the research will have no part in determining the viability of a neonate. Rather, an independent examiner should determine such viability/nonviability.

Neonates of Uncertain Viability: Until it has been determined whether or not a neonate is viable, the IRB may approve research involving these neonates of uncertain viability, only if it determines and documents (pursuant to 45 CFR 46.205) that:
   1a) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective; OR
   1b) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; AND
2) The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with the UM written policies and procedures (contained herein) on informed consent, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

**Nonviable Neonates:** The IRB may approve studies involving post-delivery, nonviable neonates only if ALL of the following additional conditions of 45 CFR 46.206 are met and documented.

1) Vital functions of the neonate will not be artificially maintained; AND
2) The research will not terminate the heartbeat or respiration of the neonate; AND
3) There will be no added risk to the neonate resulting from the research; AND
4) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; AND
5) The legally effective informed consent of both parents of the neonate is obtained in accord with these UM written policies and procedures, except that the waiver and alteration provisions of 45 CFR 46.116 (c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

**Neonates of Uncertain Viability and Nonviable Neonates:** The IRB may approve studies involving neonates of uncertain viability and nonviable neonates only if all of the following conditions are met and documented:

1) Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates; AND
2) Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate; AND
3) Individuals engaged in the research will have no part in determining the viability of a neonate; rather, an independent examiner should determine such viability/nonviability; AND
4) The requirements pertaining to neonates of uncertain viability and nonviable neonates that are contained in other sections of these policies and in 45 CFR 46.205 (b) and (c) have been met as applicable.
23.4 PRISONERS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: April 24, 2006

23.4(A) GENERAL PRINCIPLES
For purposes of these policies, "prisoners" are defined either as:
1) Individuals involuntarily confined, detained, or incarcerated in a penal institution or other alternative facility (by virtue of criminal or civil statutes or commitment proceedings that provide alternatives to criminal prosecution or incarceration in a penal institution); OR
2) Individuals detained pending arraignment, trial, or sentencing

Federal, state and local regulations and the policies pertaining to human subjects in research that are included in other sections of this document are applicable also to research involving prisoners. However, federal regulations define increased safeguards that must be provided to biomedical and behavioral research involving prisoners as subjects. These additional regulations and the ethical standards of the University of Miami include the prison setting and/or subjects who are:
1) Prisoners at the time of the study
2) Subjects who become prisoners following their enrollment in the study
3) Subjects for whom being a prisoner is coincidental with their research involvement (e.g. a prisoner with cancer enrolled in a treatment oriented study that involves no other prisoners)

[NOTE – If an adolescent were to be a prisoner such as through detention in a juvenile detention facility, Subpart D of the federal regulations and the UM policies that pertain to children (see below) shall apply in addition to Subpart C and the UM policies that pertain to prisoners]

Prisoners are considered a vulnerable population because their incarceration and the constraints imposed on them during their incarceration could affect their ability to make a truly informed, voluntary and uncoerced decision whether or not to participate as subjects in research. The IRB shall understand that prisoners are in a restrictive institutional environment that affords little opportunity for making choices, earning money, communicating with outsiders, or obtaining medical care. Because their autonomy is limited, prisoners may participate only in certain categories of research, and special precautions are needed to assure that their consent to participate in the research is both knowing and voluntary.
23.4(b) IRB REVIEW OF RESEARCH INVOLVING PRISONERS

In addition to satisfying the general requirements for IRB review of research as defined in federal regulations and in these written policies and procedures, an IRB must meet the following requirements when reviewing studies involving prisoners including initial applications, continuing reports, amendments and unanticipated problems:

1) A majority of the IRB (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the IRB; AND

2) At least one member of the IRB shall be a prisoner, or a prisoner representative with appropriate background, relevant experience and a close working knowledge, understanding and appreciation of prison conditions from the perspective of the prisoner to serve in that capacity, except that where a particular research project is reviewed by more than one IRB, only one IRB need satisfy this requirement

Convened IRB review shall be a standard for all studies involving prisoners. Regulations do not permit the IRB to categorize and approve prisoner research as exempt [45 CFR46.101 (i, footnote 1)]. Expedited review may be appropriate in limited circumstances such as if the study is restricted to a retrospective review of prisoner records or it constitutes only minor modifications to previously approved prisoner research or if the study would otherwise qualify for exemption (i.e. data registry). If a research study involving prisoners does qualify for expedited review, a prisoner representative should be one of the designated reviewers. In all cases, all required findings must be addressed and documented and a report made to the convened IRB.

Allowable Categories of Prisoner Research: IRB approval of studies involving prisoners may be given if such studies involve solely at least one of the four allowable categories expressed in federal regulations [45 CFR 46.306]. The Principal Investigator shall recommend the applicable category as part of his/her submission to the IRB. The four permissible categories are:

1) The study is of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subject [NOTE – Minimal risk for prisoner research is defined as the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of health persons.]

This definition is distinct from the definition of minimal risk applied to studies that do not involve prisoners. For the latter studies, federal regulations [45 CR 46.102] define minimal risk as being "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."

2) The study is of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subject
3) The study is on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary of Health and Human Services (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research.

4) The study is on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary of Health and Human Services (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research.

Another category of research that may be permissible was added by recent federal regulations. This pertains to Epidemiological Research which is defined as ‘public health research that focuses on a particular condition or disease in order to (i) describe its prevalence or incidence by identifying all cases, including prisoner cases, or (ii) study potential risk factor associations, where the human subject may include prisoners in the study population but not exclusively as a target group provided that the study presents no more than minimal risk and no more than inconvenience to the subject (see definition of minimal risk unique to prisoners, above).

Seven Required Findings to Approve Prisoner Research: If the IRB determines that a prisoner study is allowable based on the categories defined above, then the IRB may approve the study if it determines and documents that all of the following seven findings are applicable to the study. These seven required additional findings [45 CFR 46.305] are:

1) The study under review represents one of the four categories of research permissible under 45 CFR 46.306 [see above]; AND

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

3) The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers; AND
4) Procedures for the selection of subject within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the Principal Investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project; **AND**

5) The information is presented in language which is understandable to the subject population; **AND**

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

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

**23.4(C) SUBJECT BECOMES A PRISONER DURING AN ON-GOING STUDY**

If a research project is ongoing, with IRB approval, and one or more of the currently enrolled subjects happens to become incarcerated or otherwise meet the definition of "prisoner", the research with that prisoner/subject (including all research interactions and interventions with, and obtaining identifiable private information about the prisoner) must immediately cease (during the entire time of incarceration) unless the following conditions are met:

1) The Principal Investigator (in his/her professional opinion) has determined that it is in the best interest of the research subject to continue
2) The prisoner/subject wishes to continue as a study participant
3) The IRB Chair has determined that the subject may continue to participate in the study until the convened IRB has re-reviewed the study
4) The convened IRB approves the study as permitting the involvement of prisoners based on the policy, criteria and findings described above

If the Principal Investigator has determined that it is in the best interest of the research subject to continue his/her participation in the study and the prisoner/subject wishes to continue as a study participant, the Principal Investigator must notify the HSRO in writing of this decision within 5 working days of learning of the change in the subject’s status to that of prisoner. Within this time also, the Principal Investigator must attach a justification including the decision of the prisoner/subject, the form necessary to amend the approved study application. This amendment shall include the additional information necessary for IRB re-review of the study for the involvement of prisoners and information and documents pertinent to the re-consent process.
For its review, the convened IRB shall follow the policies on prisoner research detailed above including that its approval shall be contingent upon its determination and documentation that the study falls into one of the four approved categories that define allowable prisoner research and that the study includes all of the seven additional findings required of the IRB.

In the interim between the principal investigator's decision to continue the participation in research of the newly defined prisoner and the review and approval of the convened IRB, the IRB Chair shall decide whether the subject/prisoner may continue to participate in the research. This decision shall be made by the IRB Chair in a timely manner upon his/her receipt of the required documentation from the HSRO.

**23.4(d) **Adding a Prisoner Component to an On-Going Study

If the Principal Investigator identifies a potential need to include prisoners in future recruitment efforts within an on-going study that had not been approved for the involvement of prisoners, the Principal Investigator must submit to the HSRO for forwarding to the IRB an amendment application. This application shall include the additional information necessary for IRB re-review of the study for the inclusion of prisoners. For its review, the convened IRB shall follow the policies on prisoner research detailed above including that its approval shall be contingent upon its determination and documentation that the study falls into one of the four approved categories that define allowable prisoner research and that the study includes all of the seven additional findings required of the IRB.

**23.4(e) **DHHS-Sponsored Studies Involving Prisoners

If the IRB approves a study involving prisoners, and if the study is supported by the U.S. Department of Health and Human Services, the study must be submitted to the Secretary of Health and Human Services for approval [c.f. 45 CFR 46.306]. The HSRO shall not issue IRB approval for the study, and the study may not be initiated, until approval is given by the DHHS Secretary.

The HSRO shall be responsible to provide documentation to the DHHS Secretary (through OHRP) necessary to certify that the IRB has appropriately reviewed and approved the research pursuant to regulations and UM policies. This documentation shall address all areas required by the OHRP guidance including the name of the research study, and any relevant HHS grant application or proposal. Also included within this information shall be:

1) A copy of the grant application including all detailed budgetary pages
2) A copy of the IRB minutes relevant to the discussion of the study. These should include information on the specific categories of research and the findings pertinent to prisoners
3) A copy of the IRB approval letter
4) A copy of all consent forms
5) The NIH Program Office name and contact information
6) A copy of any application forms required by the IRB
7) Any other information requested or required by the IRB to be considered during initial review
8) A certification affirming that the IRB approved the research and fulfilled its duties under 45 CFR 46.305
The DHHS Secretary (through OHRP) shall determine whether the proposed study falls within the categories of permissible prisoner research. Upon certification by the DHHS Secretary that the research fits into the prisoner category and that the IRB findings have been documented, the DHHS shall issue a certification letter for the IRB. Upon receipt of the certification letter, the HSRO may issue an approval. [NOTE – This certification process only applies to DHHS-sponsored research, unless the Principal Investigator identifies another certification process as required by a sponsor]
23.5 CHILDREN

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: October 16, 2006

23.5(a) GENERAL PRINCIPLES, CONSENT AND ASSENT

Federal regulations [45 CFR 46, Subpart D and 21 CFR 50, Subpart D] and University ethical standards require that Principal Investigators and the IRB shall be sensitive to the vulnerability of subjects who are children and apply special conceptual and regulatory protections to research involving children. Principal Investigators and the IRB shall also be responsive to the need to include children in human subject research unless there are scientific or ethical reasons not to include them.

OHRP/FDA defines "children" as persons who have not attained the legal age for consent to treatments or procedures involved in the research/clinical investigations, under the applicable law of the jurisdiction in which the research/clinical investigation will be conducted. The age of majority in the State of Florida is eighteen (18) [§743.07].

Consent: For subjects under 18 years of age, consent must be obtained from the child's biological or adoptive parents or court-appointed legal guardian. A court-appointed legal guardian must obtain court approval to provide consent for a child to participate in research studies. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient if: a) the research does not involve greater than minimal risk; or b) the research involves more than minimal risk but presents the prospect of direct benefit to the individual child. If the research does not fit within one of the two categories and consent is to be obtained from parents, both parents must give consent unless one parent is deceased, unknown, incompetent, or not reasonably available or unless only one parent has legal responsibility for the care and custody of the child [45 CFR 46.408].

The IRB may approve a waiver of the consent requirements for studies involving children if the conditions for waivers of other studies are met [see policy on Informed Consent and 45 CFR 46.116] and if the IRB determines that the study is designed for conditions or for a subject population for which parental or guardian consent is not a reasonable requirement to protect the subjects (for example, neglected or abused children). The granting of a waiver of consent may be made if the IRB approves the substitution of an appropriate mechanism for protecting the children who will participate as subjects in the research and provided further that the waiver is not inconsistent with Federal, state or local law. The choice of an appropriate mechanism shall depend upon the nature and purpose of the activities described in the protocol the risk and anticipated benefit to the research subjects, and their age, maturity, status and condition.
Assent: In addition to the consent of parents or the legal guardian, the IRB shall require, from children 7 through 17 years of age and who, in the judgment of the IRB, are capable of providing assent, the child’s affirmative agreement (assent) to participate in research. In the absence of affirmative agreement, the child’s failure to object to research participation should not be considered as assent.

In determining whether children are capable of assent, the IRB shall take into account the ages, maturity, and psychological state of the children involved (45 CFR 46.408, 21 CFR 50). This judgment may be made for all children to be involved in research within a particular study, or for each child, as the IRB deems appropriate.

The assent of child-subjects is not a necessary condition for proceeding with a study if the IRB determines either of the following:

1) The capability of some or all of the children is so limited that they cannot reasonably be consulted; OR
2) The intervention or procedure in the study 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.

Even if the IRB determines that the participants are capable of assenting, the IRB may waive the assent requirement if it finds and documents that:

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

The IRB shall determine whether and how assent must be documented. The process for obtaining assent from children shall include a brief description of the study. This description should be appropriate to the level of reading and understanding of the child and should be followed by the statement such as:

I agree _______ I do not agree ________ to participate in this study which I have read or which has been explained to me by ____________________

Signature and date lines for the child, parent, and the person obtaining assent are needed.
23.5(B) IRB REVIEW OF RESEARCH INVOLVING CHILDREN

In addition to the general review conditions defined within regulations and the policies contained in this document that pertain to all studies, the IRB may approve a study involving children only if there are adequate provisions for soliciting the assent of the children and the permission of their parents or guardians (see above) and only if such research fits within one of the categories permitted by federal regulations (45 CFR 46.404-407 and/or 21 CFR 50.51-54. These categories are:

1) The research involves no greater than minimal risk
2) The research involves greater than minimal risk, but presents the prospect of direct benefit to an individual subject. Research in this category is may be approved if the IRB determines the following:
   a. The risk is justified by the anticipated benefit to the subjects; AND
   b. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches
3) The research involves greater than minimal risk and no prospect of direct benefit to individual subjects, but the research is likely to yield generalizable knowledge about the subject's disorder or condition. Research in this category may be approved if the IRB determines the following:
   a. The risk represents a minor increase over minimal risk; AND
   b. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational situations; AND
   c. The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition that is of vital importance for the understanding or amelioration of the subjects' disorder or condition
4) The study is not otherwise approvable but the research presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children. A study determined by the IRB to be in this category may be approved by the IRB if the IRB determines 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. However, the HSRO shall not issue IRB approval for the study, and the study may not be initiated, until a determination is issued by the Secretary of the U.S. Department of Health and Human Services concurring with the determination of the IRB.

To obtain approval by the DHHS Secretary, the HSRO shall provide all required documentation (through OHRP).

If the IRB approves a study involving prisoners, and if the study is supported by the U.S. Department of Health and Human Services, the study must be submitted to the Secretary of Health and Human Services for approval [c.f. 45 CFR 46.306]. The HSRO shall not issue IRB approval for the study, and the study may not be initiated, until approval is given by the DHHS Secretary.
The HSRO shall be responsible to provide required documentation to the DHHS Secretary (through OHRP) necessary to decide whether the IRB has appropriately reviewed and approved the research pursuant to regulations and UM policies. The DHHS Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, shall issue a determination which, if positive, will permit the HSRO to issue a letter to the Principal Investigator approving the study.

In assessing benefits and the probability and magnitude of risk to children especially in health care situations, Principal Investigators and the IRB should consider the current and anticipated health status and emotional maturity of the child, the risks and discomforts inherent in the proposed research and the burden regardless of whether the child is accustomed to the proposed procedures. In assessing risks in non-health care related (social science) research involving children, Principal Investigators and the IRB should consider that risks may be emotional/psychological or to social standing. An IRB member or consultant with appropriate background and experience in Pediatrics or a related topic should participate in the IRB’s calculation of the risks and benefits with consideration of the circumstances of the subjects under study.

23.5(C) WARDS OF THE STATE OR OTHER AGENCY, INSTITUTION OR ENTITY

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: June 28, 2006

In general, a 'ward' is a child (or adult) whose welfare is the responsibility of the State or any other agency, institution or entity. For example, the FDA [21 CFR 50.3(q)] defines a ward as a "child who is placed in the legal custody of the State or other agency, institution, or entity, consistent with applicable Federal, State or local law" while Florida Statute 755.102(2) defines a ward as "a person for whom a guardian has been appointed." This policy applies to wards of the State or other agency, institution or entity who are children or adults. Such individuals can be included in research studies approved pursuant to these policies [c.f. 45 CFR 46.409, 21 CFR 50.56] only if such research is either:

1) Related to their status as wards; OR
2) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards

A principal investigator seeking to enroll a ward of the state in a research study must contact the agency/individual that has jurisdiction/guardianship of the ward to determine the status of the parental rights and whether or not a guardian has been appointed in order to seek permission and to obtain any relevant court orders. Depending on the status of parental rights, the investigator must also seek authorization from the Court before the ward may participate in the study. In order to accomplish the latter, the investigator must justify the requirements of Florida Statues (see below).
If parental rights have not been terminated, investigators must involve the parent(s) in the decision-making process unless appropriate court documents are presented that define any custody issues that eliminate the requirement that the non-custodial parent be present. Even where parental rights are still partially intact, however, investigators may still be required to provide the IRB with appropriate court documents that demonstrate that authorization to allow the ward to participate in the research study was granted by the Court.

If the IRB approves a study involving wards of the State, the IRB shall require appointment of an advocate for each child who is a ward. The advocate shall serve in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and who agrees to act in, the best interest of the child for the duration of the child's participation in the research. The advocate may not be associated in any way (except in the role as advocate or member of the IRB) with the study, the investigator(s) or the guardian organization.

Additional regulatory requirements are defined under title XLIII, Chapter 744 of the Florida Statutes. These are as follows:

**744.3215 – Rights of Persons Determined Incapacitated:**

a. Without first obtaining specific authority from the court as described in 744.3725 (procedure for extraordinary authority) a guardian may not:

b. Consent on behalf of the ward to the performance on the ward or to the participation by the ward in any biomedical or behavioral experiment or procedure

Under Florida Statute 744.32215(4)(b), the court may permit such performance or participation by the ward only if:

a. It is of direct benefit to, and is intended to preserve the life of or prevent serious impairment to the mental or physical health of the ward; OR

b. It is intended to assist the ward to develop or regain his or her abilities
744.3725 -- Procedure for Extraordinary Authority
Before the Florida court may grant authority to a guardian to exercise any of the rights specified in 744.3215(4), the court must:

a. Appoint an independent attorney to act on the incapacitated person’s behalf, and the attorney must have the opportunity to meet with the person and to present evidence and cross-examine witnesses at any hearing on the petition for authority to act

b. Receive as evidence independent medical, psychological, and social evaluations with respect to the incapacitated person by competent professionals or appoint is own experts to assist in the evaluations

c. Personally meet with the incapacitated person to obtain its own impression of the person’s capacity, so as to afford the incapacitated person the full opportunity to express his or her personal views or desires with respect to the judicial proceeding and issue before the court

d. Find by clear and convincing evidence that the person lacks the capacity to make a decision about the issue before the court and that the incapacitated person’s capacity is not likely to change in the foreseeable future

e. Be persuaded by clear and convincing evidence that the authority being requested is in the best interests of the incapacitated person
23.6 Decisionally Impaired Subjects

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: April 24, 2006

Decisionally impaired persons are those who have a diminished capacity for rationally and autonomously providing informed consent due to a psychiatric, organic, developmental or other disorder that affects cognitive or emotional functions. The diminution of capacity may be a temporary impairment such as from physical trauma or emotional-stress; or it may be chronic impairment such as from neurologic, psychiatric or substance abuse problems.

A distinction should be made between the legal meaning of the term "incompetent" and the broader term "decisionally impaired". Many decisionally impaired individuals have been declared "incompetent" by a court of law with the appointment of a legally authorized representative for the individual judged incompetent by the court; but this declaration is not necessarily the case for all decisionally impaired persons and the lack of its occurrence should not be the only indicator of decisional impairment.

The IRB shall recognize that important research questions may only be answered by studies involving subjects with impaired decision-making capacity and that precluding such research would deprive such subjects from potential study benefits including potential therapies of many disorders. As is true for almost all clinical research, it is also possible that such studies may not directly benefit the individual participant but may offer future benefits to others who have or will develop the condition or disorder. For example, genetic studies, biochemical measures, or other non-therapeutic approaches may benefit subsequent generations. While limited decision-making capacity should not prevent participation in research, the IRB shall provide additional scrutiny for research involving this population.

Informed consent for prospective research subjects who are not competent must be obtained from a legally authorized representative or health care surrogate who is specifically appointed. A signature line for the representative or health care surrogate must be added to the consent form in these cases.
Criteria for IRB approval of studies involving cognitively impaired subjects shall be defined in IRB deliberations and included in the meeting minutes. Such criteria include:

1) Cognitively impaired individuals are the only suitable research subjects or are required subjects for the study. There must be a compelling reason to include cognitively impaired subjects and such individuals must not be subjects in research simply because they are readily available

2) Whether, if the study is of more than a minor increase over minimal risk, the study holds out the prospect of direct benefit to the individual in a risk-benefit ratio at least as favorable to the subjects as that presented by available alternate approaches

3) Whether the research is intended to benefit the subjects and the probability of benefit is greater than the probability of harm

4) The Principal Investigator shall attempt to obtain assent from the potential subjects and under no circumstances shall subjects being forced or coerced to participate

5) The subjects' representatives are well informed on the proposed research and regarding their roles and obligations to protect the cognitively impaired subjects and representatives must be told that their obligation is to try to determine what the subjects would do if competent or what they think is in the subjects' best interest.

6) Whether the informed consent process can be structured to be appropriate and effective within the limits of the potential subjects' decisional capacity

The IRB shall consider the guidance of the National Institutes of Health it is review of research involving subjects who are or may be decisionally-impaired. This guidance includes:

1) The consent process and documents should clearly differentiate between individualized treatment and research and between clinician and clinical investigator. This is because cognitively impaired subjects may find it difficult to differentiate between research and treatment

2) At least one voting member of the IRB shall have the appropriate professional background or knowledge and experience working with cognitively impaired persons [45 CFR 46.107; 21 CFR 56.107]

3) The IRB shall be sensitive to the fact that decision-making capacity may fluctuate, requiring ongoing assessment during the course of the study. The consent process should be ongoing

4) The IRB shall ensure that if impairment increases, additional safeguards are in place prior to involving impaired subjects in research that poses greater than minimal risk
23.7 EMPLOYEES, STUDENTS, TRAINEES AND OTHERS

**Review Responsibility:** IRB Policy and Procedure Committee

**Current Approval Date:** April 24, 2006

The following policies apply to employees, students, trainees and others who shall be considered as vulnerable populations. It shall be recognized that some individuals for whom the following policies apply may also be included in other categories of vulnerable populations such as pregnant women, prisoners or children. Additional policies for these individuals have been defined in other sections of this document. When subjects fall within two or more vulnerable population categories, the total of regulations and policies apply to these subjects.

**Employees, students and trainees/fellows** of the University of Miami or Jackson Health System or affiliates may be considered vulnerable subjects, depending on the context of the specific research study proposed. This is because of the potential for perceived coercion due to the relationships to the institutions and to the researchers (regardless of the researcher’s intentions) especially if there is a power differential between the researcher and the prospective subjects. If the proposed subjects are part of a research team, there may also be inherent conflicts of interest in their participation.

As do others considered within vulnerable populations in federal regulations and these policies, employees, students and trainees/fellows shall have rights to participate in human subject research. The IRB shall ensure that all of the following conditions are met in determining whether such individuals may participate as subjects:

1) Participation in the research may not bestow upon the subject-employees, students or trainees/fellows any competitive academic or occupational advantage over other employees, students or trainees/fellows who do not volunteer to participate in the study.

2) Investigators or others may not impose any academic or occupational penalty on those employees, students or trainees/fellows who do not volunteer.

3) Employees, students or trainees/fellows participating in research may not be systematically treated differently from subjects in the study who are not employees, students or trainees/fellows.
Due to the potential for perceived or real coercion to participate in research studies, employees, students or trainees/fellows may not participate as subjects in studies in which the principal investigator or anyone listed as key personnel has direct supervisory responsibilities over the employee, student or trainee/fellow. The Principal Investigator may request, and the IRB may approve, a waiver of this prohibition if the following conditions are documented to apply:

1) Participation in the study is reasonably likely to provide direct and significant benefit to the subjects; AND
2) Risks to the subjects have been eliminated or have been minimized to the satisfaction of the subjects; AND
3) The study has reasonable scientific merit

**Other vulnerable subjects:** The IRB shall take into account subject vulnerability from such factors as socioeconomic circumstances, cultural or religious background and personal or family circumstances. Examples of concerns that should be considered by the IRB include:

1) Financial compensation offered to impoverished subjects for participation in research may be interpreted as exploitative
2) Local cultural leaders may urge participation in a study which may be perceived as exploitative
3) Individuals in the midst of traumatic or emergency situations may be under emotional distress and increased vulnerability
SECTION 24: CONFIDENTIALITY AND CERTIFICATES OF CONFIDENTIALITY
24.1 WHICH POLICIES MUST BE FOLLOWED

IRB approval of all studies shall include review of, and be contingent upon, appropriateness, of strategies to ensure privacy, security and confidentiality of information acquired within the research. In those studies involving protected health information (PHI - see definition below), there are additional requirements set forth by HIPAA regulations which also must be followed; and where applicable, IRB approval shall include review of, and be contingent upon, compliance with HIPAA regulations as well as with federal, state and local regulations and institutional policies.

Determining whether a study must be compliant with HIPAA regulations is complicated. This is because a study could involve health information that is included within the definition of PHI (i.e. the study falls under HIPAA regulations) while another study could involve similar health information and not be under HIPAA regulations because the health information fits the definition of “Research-Related Health Information” (RHI – see definition below). The following summary provides guidance to determine whether a study requires compliance with HIPAA regulations. If an investigator is unsure if his/her research study requires HIPAA compliance, he/she should contact the HSRO prior to submitting a study application to the IRB.

UM investigators who do not access or create health information from/with the “covered entity” (i.e. they are acting solely as researchers and not as health-care service providers) are not considered part of the UM or JHS “covered entity” and are not subject to HIPAA regulations. Such investigators (and their studies) must be compliant only with applicable state privacy laws and institutional and IRB policies regarding privacy, security and confidentiality. This is because the University of Miami is a “hybrid covered entity” with certain health care components (UM hospitals and clinics) covered by HIPAA under the “covered entity” and research components that may not be covered by HIPAA or that fall outside of the “covered entity”.

However, UM investigators who obtain or access PHI from a “covered entity,” or who create, use or access health information while providing health care services to research subjects, must comply also with HIPAA regulations and the HIPAA-related, privacy and security policies of the “covered entity”, the institution and the IRB as well as state law. This HIPAA requirement applies no matter whether PHI is obtained, accessed or created preceding the conduct of a study or during the study.
The following is guidance as to which regulations and policies apply to a particular study:

1. For those studies in which: a) no health information is created, used, obtained or accessed from or on behalf of a UM or JHS covered entity; AND b) all information gathered from or about subjects will be used exclusively for the approved research (i.e. it will not be entered into any patient medical records or otherwise used for purposes of treatment or healthcare of the research participant), the investigator and his/her study must be compliant with the following policies:
   a. UM general Information Technology (IT) information and security policies: these are available at http://it.med.miami.edu/x1041.xml
   b. IRB policies on Privacy, Security and Confidentiality

2. For those studies which access, use or create protected health information (PHI) about subjects that has been or will be used both in the subject’s clinical treatment and in the research, the following policies are applicable:
   a. UM general IT information and security policies: these are available at http://it.med.miami.edu/x1041.xml
   b. IRB policies on Privacy, Security, Confidentiality and HIPAA
   c. institutional HIPAA policies (these are administered by the Office of HIPAA Privacy and Security and are available at http://www.med.miami.edu/hipaa/public/

[NOTE – Compliance with HIPAA regulations and policies is required even if only a portion of the study involves creating, accessing, obtaining, recording or deriving PHI.]

In summary, all studies in which PHI is involved (i.e. obtained, accessed, created or recorded) are subject to HIPAA regulations and applicable institutional policies. This includes clinical trials, chart reviews, epidemiological studies, behavioral and social science studies and some basic science research activities. HIPAA-applicable studies may include the provision of treatment but others may provide neither treatment nor diagnosis.
24.2 DEFINITIONS

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** August 6, 2008

Terms common to documents or discussions of privacy, security, confidentiality and HIPAA are included below. Most HIPAA-related definitions are consistent with those in the Common Rule (i.e. the human subject research regulations codified by federal agencies). In situations where there may be ambiguity or inconsistency in these definitions, the language of the applicable regulation (i.e. the Common Rule or HIPAA) shall govern.

**Confidentiality:** the condition in which information is shared or released in a controlled manner. Information considered confidential should be protected against theft or improper use and should not be made available or disclosed to unauthorized individuals, entities or processes without express permission from the appropriate party.

**Covered Entity:** a health plan, a healthcare clearinghouse or a healthcare provider who is required to comply with HIPAA regulations regarding the use and disclosure of Protected Health Information (PHI).

**Data Use Agreement:** An investigator-submitted agreement required for the disclosure of a limited data set by a covered entity to the investigator. The agreement must specify the permitted uses of the limited data set and who may use or receive the data set. The agreement restricts further use and disclosure and restricts re-identification of the data or contact with subjects.

**De-Identified Information:** health information is considered de-identified (and therefore, not PHI) if the following apply:
   a. it does not identify an individual
   b. the covered entity has no reasonable basis to believe that the information can be used to identify an individual.
c. if the HIPAA-defined, 18 standard identifiers are removed from the health information and if the remaining health information could not be used alone, or in combination, to identify a subject

**NOTE – the 18 standard identifiers which must be removed for data to be considered “de-identified” are:**

1. names
2. geographic subdivisions smaller than a state
3. dates including birth date, admission date, discharge date, date of death, and all ages over 89,
4. telephone numbers
5. fax numbers
6. electronic mail addresses
7. Social Security numbers
8. medical record numbers
9. health plan beneficiary numbers
10. account numbers
11. certificate/license numbers
12. vehicle identifiers and serial numbers, including license plate numbers
13. device identifiers and serial numbers
14. Web Universal Resource Locator (URL)
15. biometric identifiers, including finger or voice prints
16. full face photographic images and any comparable images
17. Internet Protocol address numbers
18. any other unique identifying number characteristic or code

**ePHI:** electronic PHI (i.e. a subset of PHI)

**HIPAA:** the federal Health Insurance Portability and Accountability Act. This act regulates, among other things, the maintenance and disclosure of protected health information (“PHI”), which includes ePHI, about patients treated by “covered entities”. In addition, this act prescribes a process through which researchers may obtain or create PHI about patients who are also research participants or potential research participants

**Hybrid Entity:** a single, legal entity that uses or discloses PHI for only a part of its business operations. The Privacy Rule applies only to the healthcare components of a hybrid entity that use or disclose PHI.
**Limited Data Set.** health information that a covered entity may disclose (pursuant to a data use agreement) to an investigator for research purposes based on the fact that certain direct identifiers have been removed. The investigator receiving the limited data set must submit the data use agreement signed by an authorized UM official and obtain IRB approval before obtaining the limited data set for use in his/her study

**NOTE – direct identifiers that must be removed in order for data to be included in a limited data set are**
1. names
2. address information (other than city, state and zip code)
3. telephone and fax numbers
4. e-mail address
5. Social Security number
6. certificate/license numbers
7. vehicle identifiers and serial numbers
8. URLs and IP addresses
9. full face photos and other comparable images
10. medical record numbers, health plan beneficiary numbers and other account numbers
11. device identifiers and serial numbers

**NOTE – the following are allowed in a limited data set:**
1. admission, discharge and service dates
2. birth date
3. date of death
4. age (including age 90 or over)
5. geographical subdivisions such as state, county, city, precinct and five digit zip code

**Privacy:** an individual’s right to be free from unauthorized or unreasonable intrusion into his/her private life and the right to control access to personal information. The term “privacy” applies to persons whereas the term “confidentiality” refers to the treatment of personal information.

**Privacy and Security Rule:** standards for Privacy of Individually Identifiable Health Information, promulgated by the U.S. Department of Health and Human Services pursuant to the Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) and codified at part 160 and part 164 , subpart C (Security Standards for the Protection of ePHI) and subpart E of Title 45 of the U.S. Code of Federal Regulations (as amended from time to time)
Written Policies and Procedures for the Protection of Human Subjects in Research

**Protected Health Information (PHI):** identifiable information about the past, present, or future physical or mental health or condition (including the provision of his/her health care, insurance, payment status etc) of an individual obtained or managed by a covered entity. PHI may be information that is recorded electronically, on paper or orally. PHI must be protected from unauthorized use or disclosure by the Covered Entity under HIPAA regulations.

*Note – PHI must be identifiable information or information that may be linked to an identifier. PHI does not include de-identified information*

**Research Related Health Information—RHI:** personally identifiable information used in research that is distinct from PHI by not being associated with, or derived from, the provision of health care or payment for care.

**Security:** the safeguards placed upon the availability, integrity, and confidentiality of information to protect information from unauthorized access, disclosure, misuse and accidental damage. Safeguards may be physical, electronic, or administrative and they may control access, training, computer systems, policies and procedures, physical environment, and behaviors.

**Sensitive Information:** private and/or health care information including information relating to an identifiable individual’s private activities or practices (e.g. sexual preferences or practices; drug or alcohol treatment history; mental health or treatment history; HIV status; diagnosis information; financial information including social security numbers or health insurance data; criminal history or background etc).
24.3 GENERAL PRINCIPLES OF IRB REVIEW OF PRIVACY, SECURITY AND CONFIDENTIALITY

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** August 6, 2008

The protection of subjects in ALL STUDIES requires the assurance that privacy, security and confidentiality are appropriately managed. Principal investigators must ensure that studies include provisions for security and for ensuring the privacy and confidentiality of participants. The strategies to ensure privacy, security and confidentiality during and after the research shall be evaluated by the IRB which acts as the Privacy Board for HIPAA-related purposes, and the appropriateness of these strategies shall be a prerequisite for its study approval.

Strategies for privacy must ensure each participant's right to be free from unauthorized or unreasonable intrusion into his/her private life and the right to control access to personal information. Research procedures should be carefully designed to limit the personal information to be acquired to that which is minimally necessary and should be administered using procedures that will protect the subject's privacy.
24.4 PRIVACY (AS APPLICABLE TO ALL STUDIES)

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: August 6, 2008

The IRB shall review, and base its study approval upon, strategies proposed by the principal investigator to ensure the privacy of research subjects. Privacy issues for IRB evaluation should include (as applicable):

a. the time and place where information is provided by participants to investigators
b. the nature of information provided by participants
c. the nature of the experiences the participants will undergo as a result of the study
d. who shall receive, access and use information provided by participants
e. factors that may determine what is private to an individual such as gender, ethnicity, age, socio-economic class, education, ability level, social or verbal skill, health status, legal status, nationality, intelligence or personality
f. the participant’s relationship to the investigator
g. the presence of others (such as parents) during data gathering

Studies requesting the use of existing, identifiable subject information for research other than that contemplated by the originally approved research protocol require IRB examination of the risks involved. The IRB shall determine whether the new use is within the scope of the original consent or whether it is necessary to obtain additional consent.

For studies in which HIPAA regulations apply (see below), the principal investigator must obtain IRB approval and provide the privacy offices of UM and/or JHS and/or other covered entities with copies of:

a. the IRB’s determination letter; AND
b. the HIPAA Authorization forms; or documentation of a Waiver and/or Partial Waiver of HIPAA Authorization; OR
c. the IRB determination letter approving the use of a Limited Data Set; OR
d. documentation that the requirements for decedent research or research preparatory to a study have been met.

**NOTE – when privacy offices of UM and/or JHS allow an investigator access to PHI to generate his/her limited data set, the investigator will be considered a Business Associate in performing this function and a business associate agreement shall be required with signature by an authorized signatory.**
For all studies involving PHI (with the exception of those creating limited or de-identified data sets) the principal investigator must assure, for IRB approval, that only the minimum necessary information is being requested and that any PHI created for research will be entered into the medical record or Designated Record Set.
24.5 HIPAA-RELATED PRIVACY POLICIES (APPLICABLE TO STUDIES INVOLVING PHI AND HIPAA)

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: August 6, 2008

24.5(a) GENERAL PRINCIPLES OF HIPAA AND PHI

The Privacy and Security Rule, at 45 CFR parts 160 and 164, establishes a category of health information, defined as protected health information (PHI), which a covered entity may use or disclose to others only in certain circumstances and under certain conditions. PHI is a subset of what is termed individually identifiable health information. With certain exceptions, individually identifiable health information becomes PHI when it is created or received by a covered entity.

The following policies, providing additional protections under federal Privacy Rules, apply to studies involving protected health information (PHI). They pertain to investigators seeking to obtain or create PHI from, or in association with, healthcare providers (“covered entities”), affiliated investigators and/or from or on behalf of a third party (e.g. an industry sponsor etc) for purposes such as:

- identifying and contacting individuals to enroll them in a research study
- creating, using and/or disclosing PHI within the context of a research study

The IRB shall review and approve studies involving PHI in accord with applicable federal, state and local laws, regulations and institutional policies on privacy, security and confidentiality including those promulgated under HIPAA.

All PHI created within a study protocol (such as when treatments are being compared), should be included in the subject’s medical record maintained by the covered entity.

24.5(b) OBTAINING PHI TO PREPARE FOR RESEARCH – PARTICIPANTS NOT YET IDENTIFIED

Investigators may wish to obtain and review information about potential participants to prepare for research. Examples of such preparatory activities include:

- developing a research protocol
- identifying potential research participants
- identifying potential clinical trial sites
HIPAA regulations limit but do not preclude the use and disclosure of PHI to prepare for research provided the activity has approval by:

a. the covered entity in situations wherein the research preparatory activity is preliminary and does not yet involve a protocol; OR
b. the IRB and the covered entity in situations wherein the research preparatory activity is defined by a protocol

This requirement for appropriate approval applies even to clinicians wanting to review records from their own patients for research purposes. IRB and/or the covered entity may approve activities preparatory to research only if investigators and/or sponsors respect these limitations [c.f 45 C.F.R. §§ 164.512(i)(1)(ii), 164.512(i)(2), 164.502(1)(i), 164.528].

Investigators seeking to obtain PHI within a protocol that is preparatory to research must submit to the HSRO a signed form entitled "Investigator Certification for Reviews Preparatory to Research" (HIPAA FORM 'E'). By submitting this Certification, the investigator must affirm that:

a. access to the patient information is sought only to prepare for research; AND
b. the requested information is necessary for this purpose; AND
c. no patient information will be copied or removed from the premises of the covered entity during or following the review

NOTE – If an electronic record is accessed remotely, the patient information may be viewed but may not be printed, copied, downloaded, or otherwise recorded for any research-related purpose.

The IRB Chair or Chair designee shall review the Certification (HIPAA Form E) and may approve the activity on behalf of the IRB. IRB approval based on HIPAA Form E permits only limited access to PHI which may not be copied or removed from the covered entity. If not approved or upon reviewer decision, the Certification shall be forwarded to the convened IRB for its review and determination. These decisions shall be forwarded in writing to investigators by the HSRO. Investigators may not initiate activities permitted by HIPAA Form E until written confirmation of IRB approval is received.

It is possible that investigators may require disclosure of PHI beyond that permitted by HIPAA Form E to identify and contact potential study participants. To accomplish this, investigators must submit a "Partial Waiver of Authorization" form (HIPAA Form F) to the HSRO.

NOTE – if a "Partial Waiver of Authorization" form (i.e. HIPAA Form F) is submitted, investigators are not required to submit the "Investigator Certification for Reviews Preparatory to Research" (HIPAA Form E).

The IRB Chair or Chair designee shall review and may approve, on behalf of the IRB, the request for a Partial Waiver of Authorization. If not approved or upon reviewer decision, the request shall be forwarded to the convened IRB for its review and determination. These decisions shall be forwarded in writing to investigators by the HSRO. Investigators may not initiate activities permitted by the Partial Waiver of Authorization until written confirmation of IRB approval is received.
24.5 (c) **Obtaining or Creating PHI to Conduct Research – Participants are Identified or Identifiable**

This subsection applies to studies that obtain or create PHI to conduct research. It does not apply to studies that create “Research Related Health Information” (RHI). Although RHI may be personally identifiable, it is not considered PHI because it is created exclusively for the study and is not derived from a healthcare service event (i.e., the provision of health care or payment for care). Also unlike PHI, RHI shall not be added to the participant’s healthcare record within a covered entity.

**NOTE – If a study involves both RHI and PHI, it falls under HIPAA regulations and related institutional policies**

Unless the IRB approves otherwise, investigators must obtain written individual authorization from each participant (or the participant’s legal representative) to access, create and/or disclose the participant’s PHI for research. The covered entity may disclose PHI to an investigator without patient authorization only if one of the follow applies:

- a. the IRB has approved a Waiver of Authorization; OR
- b. the IRB has approved that the study may use a Limited Data Set and there is a Data Use Agreement between the investigator and the covered entity; OR
- c. the covered entity has approved an activity or the IRB has approved a protocol as preparatory to research; OR
- d. the research is being conducted with PHI from decedents and Form D is provided; OR
- e. the IRB has approved that the study may use de-identified data.

The HIPAA requirement for patient/participant authorization is additional and independent to the Common Rule requirement for informed consent and is not affected by an IRB decision to waive informed consent. Investigators who access PHI generally must obtain both HIPAA authorization and informed consent from study participants.

The research authorization form (HIPAA-Form B) is different from the consent form. The authorization form (and the process by which authorization is obtained from participants) should be submitted with a study application for IRB review and approval which shall be based on HIPAA regulations and other applicable Florida and federal laws. The authorization document should describe who may receive, use, and disclose the participant’s PHI, the purposes for which the information may be used and disclosed, and the participant’s rights with respect to these uses and disclosures of his/her PHI.

Patient/participant authorization is study-specific and applies only to PHI for the IRB-approved study. Subsequent uses or disclosures of this information for other research purposes require a new authorization or waiver of authorization by the IRB.

PHI previously disclosed by a covered entity may be subsequently used for studies other than that originally approved by the IRB or disclosed to a third party sponsor. This requires either:

- a. a new, IRB approved HIPAA authorization; OR
- b. an IRB approved waiver of authorization with an IRB-approved informed consent document that defines that participants permit the use of this information for future, unspecified research activities
Authorization may not be combined with any other document, including the informed consent or an authorization to use or disclose the patient information for another study, or an authorization to place the information in a database or repository for future analysis that is not part of the original protocol (even if informed consent is obtained for both the initial and future analyses).

24.5(c)(1) Obtaining HIPAA Authorization
Authorization is the process through which participants allow investigators to access their protected health information (PHI). The authorization process is similar to that used to obtain informed consent. For each, investigators must be prepared to explain to potential research participants the purpose and meaning of the authorization form. The authorization must be in writing unless the IRB waives this requirement.

Information conveyed to participants in authorization forms and in the process of obtaining authorization must describe what PHI will be used in the research and the purpose of that PHI in the research and who may receive, use or disclose the information. Authorization must include an expiration date or event (if the information will be kept indefinitely, the authorization should state that there is no expiration date). Authorization forms and process must include the right to revoke or refusal to sign authorization and may include that the subject’s rights to access his/her PHI will be suspended while the study is in progress but will be reinstated at the conclusion of the study.

If individuals refuse to sign authorization, they may be excluded from the research and any treatment associated with the research.

Blanket authorizations for research to be conducted in the future are not permitted. Each new use requires a specific authorization.

The authorization form must be signed and dated by the research participant or his or her legal representative. Generally, individuals who have appropriate authority to provide informed consent on behalf of an individual for participation in the research study may also provide authorization on behalf of that individual (note- specific details regarding signature by or for incapacitated or decisionally impaired adults, minors and vulnerable populations are included in the informed consent policies of the IRB. The policy on translations of informed consent documents and process shall also apply to translations of authorization documents and processes. The research participant must be given a copy of the signed authorization at the time of signature.

In a timely manner, investigators should place a copy of the signed authorization in the participant’s medical record. The covered entity must keep a copy of the signed authorization in the medical record for a minimum of six (6) years from (i) the signature date or (ii) when the participant’s information was last used or disclosed by the covered entity pursuant to the authorization, whichever is later.

24.5(c)(2) Waivers of Authorization
The IRB may waive the requirement for HIPAA research authorization by a determination that shall be made separately from a decision to waive informed consent. Investigators may request an authorization waiver in the initial study application; or investigators may submit an amendment requesting an authorization waiver if the waiver is being requested during an on-going study.
Waivers of authorization are study-specific. The IRB may not approve a waiver request that will permit the use of PHI for any research purpose that is not part of the original study. The Privacy Rule requires that PHI made available under a waiver of authorization be the minimum necessary data for the research purpose. The IRB shall consider this standard when determining which, if any, of the direct or indirect patient identifiers included in the definition of patient information may be necessary to the research.

The IRB may approve waivers of authorization if studies satisfy each of the following waiver criteria of the Privacy Rule:

a. The proposed use or disclosure of PHI involves no more that a minimal risk to participants’ privacy based on, at least, the following:
   1. An adequate plan to protect the identifiers from improper use and disclosure;
   2. An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research reason for retaining the identifiers or if keeping the identifiers is required by law; and
   3. adequate written assurances that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for oversight of the research, or for other research for which authorization or waiver of authorization is obtained

b. The research could not practicably be conducted without the waiver or alteration; and

c. The research could not practicably be conducted without access to and use of the PHI.

An investigator requesting a waiver of authorization must justify in the study application why a limited data set of patient information is not appropriate for the research purpose.

The IRB must document and retain copies for six years of all information that demonstrates that the Waiver of Authorization criteria were met. The covered entity must document and retain copies for six years of all IRB determination letters certifying approval of the Waiver of Authorization. The covered entity must provide an accounting or summary to the subject of any disclosures of PHI provided with a Waiver of Authorization.
24.6 SECURITY

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: August 6, 2008

24.6(A) GENERAL PRINCIPLES OF SECURITY

All research data (including PHI) must be secure and protected, as reasonable, against breaches in confidentiality such as unpermitted uses or disclosures. This includes research data and/or PHI that is stored electronically (ePHI). HIPAA standards also apply to PHI after project completion when computers, devices and/or media are destroyed or re-formatted for other uses. The UM Information Technology Office resources and policies which govern data security are available at http://it.med.miami.edu/x1041.xml

The protection of subjects in ALL STUDIES requires the assurance that there are adequate provisions to secure research data. The IRB shall review the adequacy of a study’s security provisions as a prerequisite for its approval. Submissions to the IRB should describe the methods of accessing, storing, and safeguarding research data to preserve confidentiality. This standard shall apply to initial review, continuing review, and review of modifications of research by expedited review procedures or by the convened IRB.

Guidelines for properly securing research data include the following:

1. As custodian of a study’s research data, the Principal Investigator shall ensure compliance with institutional data security policies, HIPAA regulations (if applicable) and the IRB-approved security protocol.
2. The PI must ensure that collaborative research studies involving PHI (or ePHI) from another institution (or under oversight of another IRB) are also approved by the UM IRB prior to receipt of PHI.
3. Access to research data (including ePHI) should be restricted and controlled. The PI must ensure locks on files or password or other protections (as applicable) (note – access to e PHI must be by password).
4. The PI must ensure that research data is accessed and used only by personnel authorized by the IRB (as approved study personnel) for such research activity.

Additional requirements under HIPAA for electronic protected health information (ePHI) include:

1. ePHI should contain only the individual identifiers that are minimally necessary to support the research purpose.
2. Mobile devices (laptops or PDAs) or electronic storage media (data sticks, tapes, disks) may be used for temporary storage of ePHI if they are encrypted, have automatic logoff features and can be accessed only by password.
3. ePHI transmitted via a network must be encrypted, password protected and sent only through secure channels. Such transmission should occur only under strong necessity.
4. Equipment and media that stored ePHI must be re-formatted prior to their disposal or reuse.
5. Confidentiality agreements must include commitments to store e-mails only on workstations in a secure network and to transmit ePHI only through secure channels
6. webpages storing ePHI should be accessed via secure server lines and only by user ID and role-specific passwords that provide access to selected pages.
7. ePHI entered through the web must reside within a secure network
8. home and laptop computers that access ePHI within a network must be password protected using a password different from the log-on password. E-Mail connections must be encrypted and anti-virus software or filters should be installed and appropriately updated

Additional requirements under HIPAA for securing paper records containing PHI include:
1. PHI must be stored using two-locked filing systems within a locked office or storage room
2. Shredding is required to discard printed materials containing PHI with directed identifiers
3. Paper-based PHI with direct identifiers should not be carried or sent unless necessary for approved research activities

Additional requirements under HIPAA for security Faxes containing PHI include:
1. faxes are discouraged but, if required, they must be sent and received in a secure environment
2. recipients of faxes should be alerted first that a fax is coming so the recipient can immediately secure the faxed document

Additional requirements under HIPAA for reporting breaches of privacy, unanticipated problems and reportable events related to ePHI include:
1. the Principal Investigator must timely inform the HSRO if a security breach of confidentiality has occurred
2. the HSRO will coordinate review of ePHI security breaches with ORCA, the Office of Information Technology and the Privacy Offices of UM and/or JHS as applicable
3. the HSRO shall forward all findings regarding data security breaches to the IRB for its review and determination
4. violations of HIPAA Security Rules by workforce members shall be reported to the UM Human Resources Department for review and actions pursuant to HR policies
24.7 CONFIDENTIALITY

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: August 6, 2008

24.7(a) General Principles of Confidentiality

Confidentiality of identifiable information shall be maintained unless subjects give permission to relinquish confidentiality. The more sensitive the information, the greater is the need for confidentiality. This is to protect subjects from potential harms such as psychological distress, loss of insurance, loss of employment and damage to social standing. Investigators should understand that to do other than maintain confidentiality would be inconsistent with the principles of the Belmont report requiring respect for persons and beneficence.

All information relating to research studies shall be kept secure and confidential to the extent permitted by law. However, records shall be available to the IRB and appropriate governmental agencies and authorized University employees or other agents authorized by the University. All others requesting information on research studies must obtain written approval from the Principal Investigator or the Associate Vice Provost for Human Subject Research.

Principal Investigators should design and conduct studies that protect to the fullest extent possible the participants’ and confidentiality. The Principal Investigator must comply with the UM policy entitled “Policy and Security of Confidential Health Information”.

24.7(b) IRB Review of Confidentiality

Studies must include appropriate strategies to protect the identity of human subjects and the confidentiality of research records. These strategies should cover all types of data collected, including personality inventories, interviews, questionnaires, observations, photographs and film, taped records and other stored data. Plans should explain the mechanisms devised for this purpose such as numbering or code systems or the locking of files in private offices and shall describe who has access to the data and under what circumstances a code system may be broken. Plans should also define the final disposition or destruction of such information.
The IRB shall evaluate strategies for confidentiality in its review process. The appropriateness of such strategies shall be a requirement for study approval. In its review, the IRB shall be guided by the following:

1. Questionnaires, inventories, interview schedules, and other data-gathering instruments and procedures should be carefully designed to limit the personal information to be acquired to that which is essential, and should be administered using procedures that will protect the subject's privacy.

2. Information that could reveal a subject's identity should be securely stored in files accessible only to the principal investigator and authorized staff listed in the IRB approved protocol.

3. As early as feasible, data should be coded to remove identifying information, and identifiers destroyed.

4. The identity of subjects should not be released except with their express permission. This includes through the use of audio tapes, videos, photos, or other images (e.g., MRI, CT scan) that either show the subject's face or would divulge unique or identifying features. Subjects should always be told during the informed consent process if their likeness or other unique or identifying features will be imaged and how the images will be used. Explicit consent must be obtained for any public use of such images (including uses in the classroom, on the internet, or as part of a presentation of the research results), since publication would otherwise constitute a breach of the basic confidentiality requirement.

5. Use of existing data that were originally obtained for different purposes and that involve identifiable subject information requires examination of the risks involved. The IRB must determine whether the new use is within the scope of the original consent or whether it is necessary or feasible to obtain additional consent. Anonymity of the subjects must be preserved in these cases.

24.7(c) **CERTIFICATES OF CONFIDENTIALITY**

**Certificates of Confidentiality:** Certificates of Confidentiality are issued by the National Institutes of Health (NIH) to protect the privacy and confidentiality of research subjects by protecting investigators and institutions from being compelled to release information that could be used to identify subjects.

In certain circumstances involving civil, criminal, administrative, legislative or other proceedings at the federal, state or local level, investigators and institutions may be compelled to release information that could be used to identify subjects within a research study. To ensure the privacy of research subjects, investigators and institutes may refuse to disclose any item or combination of items in the research data that could lead directly or indirectly to the identification of a research subject if protected by a Certificate of Confidentiality.
Principal Investigators may apply for a Certificate of Confidentiality from the National Institutes of Health (NIH) under section 301(d) of the Public Health Service Act [42 U.S.C. 241(d)]. A Certificate may be awarded whether or not a research project is federally funded. Certificates may be requested prior to the submission of an application for study approval to the IRB; or the IRB may require that the Principal Investigator obtain a Certificate of Confidentiality from the NIH prior to conducting the research. Generally, an application for a Certificate is submitted after IRB approval of the research because IRB approval is a prerequisite for issuance of a Certificate.

A separate application is required for each research project for which a Certificate is desired even if the projects have a common Principal Investigator. A Certificate is generally issued to a research institution for a single project (not broad groups or classes of projects). However, projects that use the same sample of subjects but have different protocols may file for one Certificate since the subjects, whose identities the investigator wishes to protect, are the same.


Certificates of Confidentiality may be issued to institutions or universities for biomedical, behavioral or other types of research where disclosure of identifying information could have adverse consequences for subjects such as by damaging their financial standing, employability, insurability, or reputation or by involving them in criminal or civil litigation. Examples of sensitive research activities that may qualify for Certificates of Confidentiality include but are not limited to:

1. Collecting genetic information
2. Collecting information on the psychological well-being or mental health of subjects
3. Collecting information on subjects' sexual attitudes, preferences or practices
4. Collecting data on substance abuse or other legal or illegal risk behaviors
5. Studies where subjects may be involved in litigation related to exposures under study (e.g. breast implants, environmental or occupational exposures)

Specific cultural or other factors may make information in other, unlisted, categories to be considered as sensitive. Certificates of Confidentiality may be granted in such cases upon appropriate justification and explanation.

Some projects are ineligible for a Certificate of Confidentiality such as those that are:

1. Not research
2. Not collecting personally identifiable information
3. Not reviewed and approved by the IRB as required by these policies
4. Collecting information that if disclosed would not significantly harm or damage the participant.
In general, Certificates are issued for single, well-defined research projects rather than groups or classes of projects. In some instances, they can be issued for cooperative multi-site projects. A coordinating center or "lead" institution designated by the NIH program officer can apply on behalf of all institutes associated with the multi-site project. The lead institution must ensure that all participating institutions conform to the application assurances and inform participants appropriately about the Certificate, its protections and the circumstances in which voluntary disclosures would be made.

A Certificate of Confidentiality protects personally identifiable information about subjects in the research project while the Certificate is in effect. Generally, Certificates are effective on the date of issuance or upon commencement of the research project if that occurs after the date of issuance. The expiration date should correspond to the completion of the study. The Certificate will state the date upon which it becomes effective and the date upon which it expires. A Certificate of Confidentiality protects all information identifiable to any individual who participates as a research subject (i.e., about whom the investigator maintains identifying information) during any time the Certificate is in effect. An extension of coverage must be requested if the research extends beyond the expiration date of the original Certificate. However, the protection afforded by the Certificate is permanent. All personally identifiable information maintained about participants in the project while the Certificate was in effect is protected in perpetuity.

Although Certificates of Confidentiality protect against involuntary disclosure, research subjects may voluntarily disclose their research data or information to physicians or other third parties and they may also authorize in writing the Principal Investigator to release the information to insurers, employers, or other third parties. In such cases, the Certificate should not be used to refuse disclosure. Moreover, Principal Investigators are not prevented from the voluntary or mandatory disclosure of matters such as child abuse, reportable communicable diseases, or a subject's threatened violence to self or others. However, if the Principal Investigator intends to make any voluntary disclosures, the consent form must specify such disclosure.

In the informed consent documents, Principal Investigators shall inform research subjects if a Certificate of Confidentiality is in effect. Subjects should be given a fair and clear explanation of the protection that a Certificate affords, including the limitations and exceptions noted above.

Certificates of Confidentiality do not authorize investigators to refuse to disclose information about subjects to the HSRO or the IRB or authorized DHHS or FDA personnel requesting such information requirements such as an audit or program evaluation.
SECTION 25: SUBCONTRACTS/AGREEMENTS FOR UM-INITIATED STUDIES THAT ENGAGE OR INVOLVE NON-UM INSTITUTIONS OR INVESTIGATORS
25.1 **GENERAL PRINCIPLES**

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** September 18, 2006

UM-initiated human subject research may take place at, or otherwise involve, a non-UM institution and/or investigator. Unless such studies are considered exempt under 45 CFR 46.101 and/or 21 CFR 56.104(d) by the UM IRB, the involvement of a non-UM institution and/or investigator in UM-initiated human studies requires that the study approval process include an agreement or subcontract with the non-UM institution or investigator. If an agreement or subcontract is required, this agreement or subcontract must be signed by the appropriate institutional officials prior to IRB approval of the study and shall be submitted by the principal investigator to the IRB as part of the study materials available for IRB deliberations.

The requirement for a subcontract/agreement applies to studies with human subjects that include a non-UM institution and/or investigator regardless of source or plans for funding.

Unless other arrangements are approved by the Associate Vice Provost for Human Subject Research to ensure research oversight at collaborating institutions, it is the responsibility of the UM IRB to review UM studies that take place at, or otherwise involve non-UM institutions and/or investigators and to determine whether these studies and the subcontract/agreement ensure optimal human subject protection. It is the responsibility of the HSRO and the Associate Vice Provost for Human Subject Research to monitor this policy and facilitate subcontracts/agreements that are required for approval of this research.

For purposes of this policy, **UM-initiated studies** are those which fit any of the following criteria:

1) The University of Miami and the UM principal investigator are recipients of the prime award (i.e. the grant supporting the research)

2) The University of Miami and the UM principal investigator are prime recipients of the funds from sponsors supporting the research

2) The University of Miami and the UM principal investigator have initiated the research and/or provide the research leadership

**NOTE – In situations where UM is a subcontractor of a study initiated by another institution, UM IRB review and approval is still required.** Documentation relating to the conduct of the study with regard to human subjects must be submitted to the HSRO.
For purposes of this policy, a **non-UM institution** is defined as an institution (or an employee or agent of the institution) that is not under the authority of UM and is located within the United States or a United States territory. Examples include clinics, schools, other universities, consulting firms or other institutions where activities include interaction or intervention with human subjects and/or the collection or analysis of identifiable data.

For purposes of this policy a **non-UM investigator** is someone not employed by or under the legal authority of UM.

This policy does not apply to non-UM institutions or facilities that are located outside of the United States and for which the "International Research Policy Involving Foreign Institutions in UM Human Subject Research" shall apply.

### 25.1(A) **RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR:**

For studies involving a non-UM institution and/or investigator, it is the responsibility of the principal investigator to:

1. Select and ensure completion and approval of an appropriate subcontract from among the five template subcontracts referenced in this policy [NOTE - See links to these subcontracts in the text below]. These templates are suggested but may be modified to meet specific circumstances
2. Ensure that the study application with protocol that is submitted to the UM IRB for review and approval describes the activities to be carried out at the non-UM institution
3. Ensure that adequate resources will be available at the non-UM institution to conduct the research safely and effectively in full accordance with the approved protocol
4. Ensure that all persons interacting with human subjects and/or with their identifiable data are adequately trained in the protection of human subjects, regardless of their employment status with UM
5. Ensure that the UM IRB receives complete reports of all IRB-reportable events occurring both at UM and at the non-UM institution
6. Ensure that consent forms fairly and accurately represent the involvement of UM in the research and the decisions of all responsible IRBs reviewing the research

Although IRB policies do not require a subcontract/agreement for exempt research involving a non-UM institution, such research may require a subcontract or other agreement from other institutional departments (e.g. UM Research Administration). It is the responsibility of the Principal Investigator to comply with such requirements.

The HSRO suggests that the UM principal investigator of an exempt study obtain a letter of permission to conduct the research activity at the non-UM institution and/or to use the resources of the non-UM institution. This documentation may be requested by the IRB during the exempt review process.
25.2 **SUBCONTRACTS FOR NON-UM INSTITUTIONS OR INDIVIDUALS “ENGAGED” IN UM RESEARCH**

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** September 18, 2006

The selection of the appropriate subcontract template from among the five subcontract templates linked within these policies depends upon whether the non-UM institution is engaged or only involved in UM research [**NOTE – Non-UM investigators who are collaborating in some way in UM research must always be considered as being "engaged" in the UM research**].

A non-UM institution is "engaged" with UM in human subject research when its employees or agents intervene or interact with living individuals for research purposes or when its employees or agents obtain identifiable private information for research purposes [45 CFR 46.102(d),(f); 21 CFR 56.102(c), (e); 21 CFR 50.3(c)(g)]. Examples of engagement may be found in the OHRP Guidance Document "Engagement of Institutions in Research". Engagement in research is contrasted with being "involved" in research. **Involvement** in research occurs when an outside institution and/or its employees or agents are not intervening or interacting with living individuals for research purposes or are not obtaining identifiable private information for research purposes (but research may be ongoing on the premises) [45 CFR 46.102(d),(f); 21 CFR 56.102(c)(e); 21 CFR 50.3(c)(g)].

Under the UM Federal Wide Assurance, UM must ensure that all institutions and investigators **ENGAGED** with UM in studies involving human subjects operate under a Federalwide Assurance (FWA) for the protection of human subjects. If the non-UM institution has an IRB or has access to an IRB, the subcontract generally will require that UM and also the non-UM institution conduct individual IRB reviews and give approval for the study. If the non-UM institution or individual has no means of access to an IRB, the subcontract may define that UM has agreed to act as the IRB of record for the study for that institution. The terms by which UM agrees to act as the IRB of record for each individual study require prior approval from the Associate Vice Provost for Human Subject Research.

For non-UM institutions and/or investigators engaged in UM human subject research, it is expected that the subcontract be constructed from the appropriate one of the following templates. However, it is recognized that in certain circumstances, these subcontracts/agreements may not be suitable. In such situations, alternative documentation may be permitted upon review and consultation with the HSRO.
**SUBCONTRACT 1:** (Template of Subcontract 1, [CLICK HERE](#))

This subcontract shall apply if all of the following apply:

1. The non-UM institution or investigator is engaged in UM research; and
2. The study is supported, at least in part, by extramural grants or sponsors
3. UM is the prime awardee of the extramural funds; and
4. The non-UM institution has its own FWA on file with OHRP and has its own IRB

It is usual that any non-UM institution with its own FWA designate its own IRB to review the research activity and approve the study in a manner additional to UM IRB review and approval. In such a dual review situation (i.e. when the UM IRB and a non-UM IRB both exercise authority for review of the study, the following conditions shall apply:

1. The non-UM institution must have an FWA
2. The UM IRB must receive reports of all IRB-reportable events occurring both at UM and at the non-UM facility
3. All non-UM site consent forms should identify the role of UM in the study

_NOTE – In some circumstances, UM may agree, pursuant to an IRB Authorization Agreement, to act as the IRB of record for a study conducted with a non-UM institution or to designate the IRB for the non-UM institution as the IRB of record for the research._

**SUBCONTRACT 2:** (For Template of Subcontract 2, [CLICK HERE](#))

This subcontract shall apply if:

1. The non-UM institution or investigator is engaged in UM research; and
2. The study is supported, at least in part, by extramural grants or sponsors
3. UM is the prime awardee of the extramural funds; and
4. The non-UM institution does not have its own FWA on file with OHRP

Non-UM institutions without their own FWA will generally be required to file an FWA and create an IRB for its own review of the collaborative UM study prior to the conduct of the research. However, there may be circumstances in which the University of Miami agrees either to extend its FWA to the non-UM institution and/or investigator for purposes of reviewing and approving the collaborative research study or to serve as the IRB of record for a non-UM institution that has an FWA but no IRB. In this circumstance, the non-UM institution must sign an IRB-authorization agreement appointing UM as the IRB of record for the study. The implementation of this option to extend the UM FWA is included in subcontract 2.
The option to extend the UM FWA to a non-UM institution requires review by the Associate Vice Provost for Human Subject Research and approval by the Vice Provost for Research. To acquire this approval, the principal investigator must submit a written request that includes a research synopsis and protocol and a description of the direct supervision and oversight of the research activities at the non-UM institution that will be provided by the UM PI and research staff. The UM PI should also describe his/her understanding of the local area context or how knowledge will be obtained (i.e. use of consultants). If the research is ongoing at another institution, the PI should provide a report on research results to date and a summary of all unanticipated problems and/or serious adverse events and other reportable adverse events. The UM IRB shall review the material and make a recommendation to the Associate Vice Provost regarding the request based upon the justification provided.

**SUBCONTRACT 3:** (For Template of Subcontract 3, [CLICK HERE](#))

This subcontract shall apply if all of the following apply:

1) The non-UM institution or investigator is engaged in UM research; and
2) The study is not supported by extramural grants or sponsors
3) The non-UM institution has its own FWA on file with OHRP and has its own IRB

As in the situation for Subcontract #1, it is expected that non-UM institutions with an FWA and an IRB will conduct their own review of the research activity and to approve the study in a manner additional to UM IRB review and approval. In such dual review situations (i.e. when the UM IRB and a non-UM IRB both exercise authority for review of the study, the following conditions shall apply:

1) The non-UM institution must have an FWA
2) The UM IRB must receive reports of all IRB-reportable events occurring both at UM and at the non-UM facility
3) All non-UM site consent forms should identify the role of UM in the study

**NOTE – In some circumstances, UM may agree, pursuant to an IRB Authorization Agreement, to act as the IRB of record for an unsponsored study conducted with a non-UM institution or to designate the IRB for the non-UM institution as the IRB of record for the research.**
**SUBCONTRACT 4:**  (For Template of Subcontract 4, [CLICK HERE](#))

This subcontract shall apply if:

1) The non-UM institution or investigator is engaged in UM research; and
2) The study is not supported by extramural grants or sponsors
3) The non-UM institution does not have its own FWA on file with OHRP

Non-UM institutions without their own FWA will generally be required to file an FWA and create an IRB for its own review and approval of the collaborative UM-initiated study prior to the conduct of the research. However, there may be circumstances in which the University of Miami agrees either to extend its FWA to the non-UM institution and/or investigator for purposes of reviewing and approving the collaborative research study or to serve as the IRB of record for a non-UM institution. In this circumstance, the non-UM institution shall sign an IRB-authorization agreement appointing UM as the IRB of record for the study. The implementation of this option to extend the UM FWA is included in subcontract 4 and requires prior review by the Associate Vice Provost for Human Subject Research and prior approval by the Vice Provost for Research in the same manner as described for subcontract 2.
25.3 AGREEMENT FOR NON-UM INSTITUTIONS OR INDIVIDUALS “INVOLVED” IN UM RESEARCH

Review Responsibility:  IRB Policy and Procedure Committee
Current Approval Date:  September 18, 2006

OUTSIDE FACILITY AGREEMENT:  (For Template of an Outside Facility Agreement, CLICK HERE)

This template agreement shall apply if the non-UM institution or investigator is involved but not engaged in UM research.  NOTE – it is recognized that in certain circumstances, this agreement may not be suitable.  In such situations, alternative documentation may be approved by the Associate Vice Provost for Human Subject Research.  Investigators are encouraged to consult with the HSRO when drafting such an agreement.

An example of a non-UM institution being "involved" in UM human subject research occurs when the non-UM institution provides a facility in which the research is being conducted or provides a pool of research participants.  This is in contrast to a non-UM institution being "engaged" in UM research because, in the former circumstance, the employees or agents of the outside facility are not intervening or interacting with living individuals for research purposes or are not obtaining identifiable private information for research purposes [45 CFR 46.102(d),(f); 21 CFR 56.102(c),(e); 21 CFR 50.3(c)(g)].
SECTION 26: INTERNATIONAL RESEARCH
26.1 GENERAL PRINCIPLES

**Review Responsibility:** IRB Policy and Procedure Committee  
**Current Approval Date:** March 7, 2007

This policy complements that contained in the previous section of the IRB Written Policies and Procedures entitled "Subcontracts/Agreements for UM-Initiated Studies that Engage or Involve Non-UM Institutions or Investigators". The former presents general principles regarding the engagement or involvement of non-UM institutions or investigators in UM studies and it includes policies related specifically to domestic sites or investigators. The present (i.e. international) policy defines additional requirements for UM-initiated human subject research taking place at, or otherwise involving, a non-UM institution and/or investigator at international sites (i.e. sites outside of the 50 states or U.S. territories).

Unless other arrangements are approved by the Associate Vice Provost for Human Subject Research to ensure research oversight at collaborating international institutions or unless such studies are considered exempt under 45 CFR 46.101 and/or 21 CFR 56.104(d) by the UM IRB, it is the responsibility of the UM IRB to review UM studies that take place at, or otherwise involve non-UM institutions and/or investigators and to determine whether the provisions in place for such international research and the subcontract/agreements ensure optimal human subject protection. It is the responsibility of the HSRO and the Associate Vice Provost for Human Subject Research to monitor this policy and facilitate subcontracts/agreements that are required for approval of this research.

For purposes of this policy, UM-initiated studies are those which fit any of the following criteria:

a) The University of Miami and the UM principal investigator are recipients of the prime award (i.e. the grant supporting the research)

b) The University of Miami and the UM principal investigator are prime recipients of the funds from sponsors supporting the research

c) The University of Miami and the UM principal investigator have initiated the research and/or provide the research leadership

**NOTE** – In situations where UM and/or a UM employee is a subcontractor of a study initiated by a foreign institution, UM IRB review and approval is still required. Documentation relating to the conduct of the study with regard to human subjects must be submitted to the HSRO.

For purposes of this policy, an international (or "foreign") institution or site is defined as an institution or site (or an employee or agent of that entity) that is not under the authority of UM and is located outside of the United States or a United States territory. Examples include clinics, schools, other universities, consulting firms or other institutions where activities include interaction or intervention with human subjects and/or the collection or analysis of identifiable health information.
For purposes of this policy a non-UM investigator is someone not employed by or under the legal authority of UM.

**Agreement or Subcontract:** As in situations involving domestic non-UM institutions and/or investigators in UM-initiated human subject research, international involvements require an agreement or subcontract with the non-UM institution or investigator. This agreement or subcontract must be signed by the appropriate officials of the foreign entity prior to IRB approval of the study and shall be submitted by the principal investigator to the IRB as part of the study materials available for IRB deliberations.

**Responsibilities:** The principal investigator and the foreign institution or site are responsible for assuring that adequate resources and facilities are available for the research. Principal investigators and the foreign institution or site are also responsible for notifying the IRB promptly if a change of research activities alters the performance entity's engagement in the research.

**Informed Consent Documents:** Informed consent documents must be consistent with requirements as defined in UM IRB policies. These requirements include that informed consent must be sought in a language understandable to the subject and under conditions that minimize the possibility of coercion or undue influence. The UM IRB shall review the informed consent documents and translations as per its written policies. Informed consent documents and translations may not be used until approved by the UM IRB.
26.2 ENGAGED IN UM-RESEARCH

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 7, 2007

When a foreign institution, site and/or investigator is to be ‘engaged” in UM human subject research, the following policies apply:

1) The research requires review and approval by the UM IRB
2) The UM IRB may approve the study if the foreign entity's procedures afford protections of the rights and welfare of the participants that are at least equivalent to those provided in 45 CFR 46, 21 CFR 50, 21 CFR 56 and the written policies of the UM IRB and if the resources and facilities are appropriate for the research.
3) The foreign institution or site must hold an FWA (“Federal Wide Assurance”) approved by the U.S. Department of Health and Human Services (DHHS), Office for Human Research Protections (OHRP) affirming that it is in compliance with DHHS regulations contained within 45 CFR 46, 21 CFR 50, and 21 CFR 56.
4) As part of its review/approval process, the UM IRB must receive and review the foreign institution or site's IRB or Independent Ethics Committee (IEC (or equivalent) review and approval of the study [NOTE – An IEC is a specially constituted review body responsible to ensure the protection of the rights, welfare and safety of research participants. An IEC shares the same composition and operations as an Institutional Review Board at a foreign site]
5) As part of its review/approval process, the UM IRB must review all subcontracts or other agreements between UM and the foreign entity and/or investigator
6) UM IRB approval is contingent upon documentation of foreign governmental approvals as applicable.
7) The study may not commence at the foreign entity or by the foreign investigator prior to UM IRB approval
26.3 INVOLVED BUT NOT ENGAGED IN UM-RESEARCH

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 7, 2007

When a foreign institution or site is involved but "not-engaged" in UM human subject research, the following policies apply:

1) The research requires review and approval by the UM IRB
2) The UM IRB may approve the study if the foreign entity's procedures afford protections of the rights and welfare of the participants that are at least equivalent to those provided in 45 CFR 46, 21 CFR 50, 21 CFR 56 and the written policies of the UM IRB and if the resources and facilities are appropriate for the research.
3) If the foreign institution or site has an established IRB/IEC or equivalent, approval of that panel must be obtained to conduct the research at the "not engaged" site or documentation must be received that the site's IRB/IEC has determined that approval is not necessary for the research to be conducted at the site
4) If the foreign institution or site does not have an established IRB/IEC, a letter of cooperation must be obtained from that institution or site demonstrating that the appropriate institutional or oversight officials are permitting the research to be conducted at the performance site
5) The UM IRB may approve the study if documentation is received from the international site's IRB/IEC determination or letter of cooperation, as applicable and if this documentation and other information deemed necessary establishes that the foreign institution's procedures afford protections of the rights and welfare of the participants that are at least equivalent to those provided in 45 CFR 46, 21 CFR 50, 21 CFR 56 and the written policies of the UM IRB and if the resources and facilities are appropriate for the research.
6) IRB approval is contingent upon documentation of foreign governmental approvals as applicable.
7) The study may not commence at the non-engaged, foreign institution or site prior to UM IRB approval.
26.4 LOCAL CONTEXT

Review Responsibility: IRB Policy and Procedure Committee  
Current Approval Date: March 7, 2007

Pursuant to regulations, OHRP guidances (8/27/1998 and 7/21/2000) and UM ethical standards, the UM IRB must possess sufficient knowledge of the local context (i.e. the institution/site and community environment) in which research for which they are responsible will be conducted. In certain circumstances, the UM IRB may rely upon the review by the local IRB for this information. However, the UM IRB must have knowledge of the local context, even if the local IRB is also reviewing the research, if either of the following applies:

1) The UM study involves research being conducted by UM employees or agents at the foreign site  
2) UM is the prime awardee on a DHHS grant and some of the funds are going to the foreign site for its engagement or involvement in the research

If neither of these circumstances apply and if the study is determined to involve no greater than minimal risk to subjects or vulnerable categories of subjects, the IRB may consider information from the local IRB as sufficient for its review of local research context.

If neither of the above circumstances applies but the study is determined to involve greater than minimal risk to subjects, the IRB shall review information regarding local context from the local IRB and from at least one additional source such as:

1) Personal knowledge from one or more IRB members, such knowledge having been obtained through extended, direct experience with the research institution, its subject populations, and its surrounding community  
2) Participation (either physically or through audiovisual or telephone conference) by one or more appropriate consultants in convened meetings of the IRB. Such consultants should have personal knowledge of the local research context, such knowledge having been obtained through extended, direct experience with the research institution, its subject populations, and its surrounding community  
3) Prior written review of the proposed research by one or more appropriate consultants, in conjunction with participation (either physically or through audiovisual or telephone conference) by the consultant in convened meetings of the IRB, when such participation is deemed warranted either by the consultant or by any member of the IRB
4) Systematic, reciprocal, and documented interchange between the IRB and elements of the local research context. Such interchange should include:
   a. Periodic visits to the research site by one or more IRB members in order to obtain and maintain knowledge of the local research context, including the research institution, its subject populations, and its surrounding community; **AND**
   b. Periodic discussion with appropriate consultants knowledgeable about the local research context; **AND**
   c. Regular interaction with one or more designated institutional liaisons; **AND**
   e. Review of relevant written materials including reports from the principal investigator or other investigators related to ongoing visits or monitoring of the foreign site

If either of the two circumstances (above) applies, the IRB shall demonstrate that it has obtained necessary information about the local research context from the local IRB and from at least one additional source (see above) and also from information from the Principal Investigator. To accomplish this, Principal Investigators should include within study applications the following information when applicable to the study:

1) Explanations of cultural and ethical differences (if any) that influenced the study design and the consent process
2) The anticipated scope of the foreign institution's or site's research activities in the UM study
3) The size and complexity of the foreign institution or site
4) Standards of professional conduct and practice of the foreign institution or site
5) The applicable commitments and regulations of the foreign institution
6) Applicable foreign law that may influence study design or conduct
7) The subject population likely to be involved in the study
8) Languages understood by the prospective subjects
9) Method for equitable selection of subjects at the foreign institution
10) A rationale for conducting the study with the foreign population
11) Method for minimizing the possibility of coercion or undue influence in seeking consent
12) Information regarding the foreign institution's or country's IRB, Ethical Review Committee or equivalent organization and its review process
13) A description of the processes for assuring confidentiality for subjects and data and the methods for transporting and securing of data to the U.S. (if applicable)
14) If subjects will receive compensation in the form of money, goods or services, an explanation is needed as to how this compensation is proportionate to the average annual income of people in the foreign country

A study shall have only one local context review unless the IRB determines that there are significant changes in the protocol or the risks to the subjects that require another local context review.
26.5 SPECIAL CONSIDERATIONS FOR INTERNATIONAL RESEARCH

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: June 5, 2007

No Written Language: For studies involving populations that have no written language an English consent form shall be used as a template for translation into the oral language. A statement translated into the foreign language must be included to explain the process of informed consent. The consent form should be signed by the interpreter, the Principal Investigator or approved designee, and the by the subject, who should be requested to make a mark or thumb print, as appropriate.

Group Consent: For studies involving populations that utilize group consent, the IRB may approve this procedure with appropriate description and written justification by the Principal Investigator for the use of group consent. The Principal Investigator should also provide a method to obtain private or individual subject assent (if possible) and a method for protecting those who choose not to participate in the study.

“Non-Therapeutic” Research: (i.e. research without the intent to produce a diagnostic, preventive, or therapeutic benefit to the current subjects, although it may benefit those with a similar condition in the future) -- Whenever possible, provisions should be made for the study population to benefit from the research study.

“Therapeutic” Research: The Principal Investigator must explain to the IRB why the study should or should not provide continued access to the experimental intervention (should it prove efficacious) or other research benefits after the completion of the study.

Studies Involving Minors (Participants under the age of 18 years): The University of Miami requirement for assent for minors in research studies are applicable for minors at foreign institutions or sites. It is usual that written, parental permission is also required. If local customs and regulations are such that active parental permission would be culturally inappropriate, a waiver of such permission may be granted at the discretion of the UM IRB providing the IRB determines that the research does not place the participant(s) at untoward risk.

Investigators seeking a waiver of parental permission must supply the IRB with proof that such permission is not culturally appropriate. Examples of such proof would be specific regulations indicating that such permission is not required, an official letter from a ranking official in the foreign country indicating that such permission is not culturally appropriate, or the appearance at a UM IRB meeting by someone of official standing in the research or academic community who can attest to the cultural inappropriateness of the requirement for active parental permission.
If a waiver of active parental permission is granted, and if a letter informing the parents of the research is deemed appropriate, it must be written at a literacy level that would be understood by the parents and translated (if appropriate) pursuant to UM policies that govern translations of informed consent and other documents. The letter should be sent to parents by the most expeditious method possible.

**HIPAA and the Collection of Protected Health Information:** HIPAA policies do not apply to those international sites not covered by HIPAA although individually identifiable health information may be collected. However, HIPAA requirements do become effective if (or when) data is transferred to a HIPAA covered entity such as a covered component of the University of Miami. No matter whether HIPAA policies are applicable or not, standard methods of protecting confidentiality and privacy for research in human subjects should apply and investigators should have these in place.

The use and disclosure of data from the University of Miami requires investigators to adhere to the Authorization requirements of HIPAA. In Studies where identifiable data will be transferred from a site not covered by HIPAA to a HIPAA covered entity, investigators should obtain HIPAA Authorizations to reduce the need to account for subsequent disclosure(s) of the PHI. Alternatively, investigators may bring data to UM either stripped of all of the 18 HIPAA identifiers with or without a code maintained at the collection site, or as a Limited Data Set with an accompanying Data Use Agreement.
26.6 SUBCONTRACTS FOR INTERNATIONAL RESEARCH

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: March 7, 2007

When a foreign institution, site or investigator will become involved in non-exempt, UM-initiated research, the study approval process shall include an agreement or subcontract with the non-UM institution or investigator. This agreement or subcontract must be signed by the appropriate officials of the foreign entity and the University prior to IRB approval of the study and shall be submitted by the principal investigator to the IRB. The requirement for a subcontract/agreement applies to studies with human subjects regardless of source or plans for funding.

Principal Investigators must select and ensure completion and approval of an appropriate subcontract from the two template subcontracts referenced in this policy (note- see links to these subcontracts in the text below). These templates are suggested but may be modified to meet specific circumstances.

Although IRB policies do not require a subcontract/agreement for exempt research involving a non-UM institution, such research may require a subcontract or other agreement from other institutional departments (e.g. UM Research Administration). It is the responsibility of the Principal Investigator to comply with such requirements.

The HSRO suggests that the UM principal investigator of an exempt study obtain a letter of permission to conduct the research activity at the non-UM institution and/or to use the resources of the non-UM institution. This documentation may be requested by the IRB during the exempt review process.

SUBCONTRACT SELECTION

Selection of the appropriate subcontract depends on whether the foreign institution or site is "engaged" or "involved in the UM-initiated study. An institution is "engaged" with UM in human subject research when its employees or agents intervene or interact with living individuals for research purposes or when its employees or agents obtain identifiable private information for research purposes [45 CFR 46.102(d),(f); 21 CFR 56.102(c),(e); 21 CFR 50.3(c),(g)]. Involvement in research occurs when an outside institution and/or its employees or agents are not intervening or interacting with living individuals for research purposes or are not obtaining identifiable private information for research purposes (but research may be ongoing on the premises) [45 CFR 46.102(d),(f); 21 CFR 56.102(c),(e); 21 CFR 50.3(c),(g)].
For a foreign institution/site engaged in UM human subject research, the subcontract should be constructed from the template labeled "INTERNATIONAL 1". This requires that the foreign institution hold an FWA and that it conduct individual IRB or IEB or equivalent reviews and give approval for the study. If the non-UM institution or individual has no means to conduct this review, the subcontract may define that UM has agreed to act as the IRB of record for the study for that institution. The terms by which UM agrees to act as the IRB of record for each individual study require prior approval from the Vice Provost for Research.

For a foreign institution/site "involved" but "not engaged" in UM human subject research, the template agreement labeled INTERNATIONAL 2 is suggested although it is recognized that in certain circumstances, this agreement may not be suitable. In such situations, alternative documentation may be approved by the Associate Vice Provost for Human Subject Research. Investigators are encouraged to consult with the HSRO when drafting such an agreement.
SECTION 27: EMERGENCY USE
27.1 GENERAL PRINCIPLES

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: August 24, 2008

FDA regulations at 21 CFR 56.102(d), 21 CFR.104(c), 21 CFR 312.36 and this policy pertain to the “emergency use”, without prospective IRB review and approval of an unapproved drug or biological product in a patient with a life-threatening (or severely debilitating) problem under the following conditions:

a. the condition is life threatening necessitating use of the test article
b. no standard acceptable treatment is available
c. there is not sufficient time to obtain prospective IRB approval.

NOTE - If IRB review is possible, prospective IRB approval should be sought. Only if treatment of a life-threatening condition is necessary before IRB approval is made, does this “emergency use” policy apply.

For purposes of this policy, “life threatening” means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted; or diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life threatening do not require the condition to be immediately life threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible. Per the FDA also, “severely debilitating” means diseases or conditions that cause major irreversible morbidity such as blindness, loss of hearing, paralysis or stroke.

Federal regulations stipulate that research activities may not be started, even in emergency situations, without prior IRB review and approval. Whenever “emergency use” of an investigational product is initiated without prior IRB approval, the patient may not be considered a research subject, the emergency treatment may not be claimed as research, and data obtained from this treatment may not be included in any report of a research activity or used for research purposes.

Federal regulations, guidance documents and this policy are not intended to limit the authority of a physician to provide emergency medical care to the extent permitted under applicable federal, state or local law [c.f. 45 CFR 46.116(f)]. Rather, this policy pertains only to the use of an investigational (i.e. “test”) article [21 CFR 56.102(l)]in emergency situations.

The emergency use of an unapproved investigational drug or biologic requires an IND unless the intended subject meets the inclusion criteria of an existing study protocol, or an approved study protocol exists. The IND requirement may be met if the manufacturer makes the drug or biologic available for the emergency use under the manufacturer’s IND.
If the emergency situation does not allow time for submission of an IND or amendment of the manufacturer’s IND, only the FDA may authorize shipment of the test article in advance of the IND submission (or amendment). Requests for such authorization may be made by telephone or other rapid communication means to the FDA [21 CFR 312.36].

**NOTE – FDA Contacts for Obtaining an Emergency IND:**

<table>
<thead>
<tr>
<th>Product</th>
<th>Office/Division to Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Products</td>
<td>Division of Drug Information (HFD-240) 301-827-4570</td>
</tr>
<tr>
<td>Biological Blood Products</td>
<td>Office of Blood Research and Review (HFM-300) 301-827-3518</td>
</tr>
<tr>
<td>Biological Vaccine Products</td>
<td>Office of Vaccines Research (HFM-400) 301-827-3070</td>
</tr>
<tr>
<td>On Nights and Weekends</td>
<td>Office of Crisis Management &amp; Emergency Operations Center (HFC-160) 301-443-1240</td>
</tr>
</tbody>
</table>
27.2 EMERGENCY USE OF UNAPPROVED MEDICAL DEVICES

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: August 24, 2008

An unapproved medical device is defined as a device that is used for a purpose or condition for which the device requires, but does not have, an approved application for premarket approval under section 515 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 360[3]). An unapproved device may be used in human subjects only if it is approved for clinical testing under an approved application for an Investigational Device Exemption (IDE) under section 510(g) of the Act (21 U.S.C. 360(i)(g) and 21 CFR part 812). Medical devices that have not received marketing clearance under section 510(k) of the FD&C Act are also considered unapproved devices which require an IDE.

The Food and Drug Administration (FDA) recognizes that emergencies arise where an unapproved device may offer the only possible life-saving alternative, but an IDE for the device does not exist, or the proposed use is not approved under an existing IDE, or the physician or institution is not approved under the IDE. Using its enforcement discretion, FDA has not objected if a physician chooses to use an unapproved device in such an emergency, provided that the physician later justifies to FDA than an emergency actually existed.

Each of the following conditions must exist to justify emergency use of an unapproved medical device:
   a. the patient is in a life-threatening condition that needs immediate treatment;
   b. no generally acceptable alternative for treating the patient is available; and
   c. because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

FDA expects the physician to determine whether these criteria have been met, to assess the potential for benefits from the unapproved use of the device, and to have substantial reason to believe that benefits will exist. The physician may not conclude that an “emergency” exists in advance of the time when treatment may be needed based solely on the expectation that IDE approval procedures may require more time than is available. Physicians should be aware that FDA expects them to exercise reasonable foresight with respect to potential emergencies and to make appropriate arrangements under the IDE procedures far enough in advance to avoid creating a situation in which such arrangements are impracticable.

In the event that a device is to be used in circumstances meeting the criteria listed above, the device developer should notify the Center for Devices and Radiological Health (CDRH) Program Operation Staff by telephone (301-594-1190) immediately after shipment is made. [NOTE - an unapproved device may not be shipped in anticipation of an emergency.] Nights and weekends, contact the FDA Office of Emergency Operations (HFA 614) 301-443-1240.
FDA expects physicians to follow as many subject protection procedures as possible. These include:
   a. obtaining an independent assessment by an uninvolved physician
   b. obtaining informed consent from the patient or a legal representative
   c. notifying institutional officials as specified by institutional policies
   d. notifying the Institutional Review Board (IRB) and
   e. obtaining authorization from the IDE holder if an approved IDE for the device exists
27.3 IRB REQUIREMENTS

Review Responsibility:  IRB Policy and Procedure Committee
Current Approval Date:  August 24, 2008

FDA regulations and UM IRB policy permit an exception to the requirement for prior IRB review and approval (21 CFR 56.104(c)) for purposes of “emergency use” if all conditions described in 21 CFR 56.102(d) exist. This exemption is allowed only for a one-time institutional use of a test article without prospective IRB review. Any subsequent use of the investigational product must have prospective IRB review and approval. If there is uncertainty as to whether emergency use of a particular investigational drug or device has occurred at UM, relevant information should be sought from the HSRO prior to the “emergency use.”

If possible prior to an “emergency use,” the physician seeking to provide the life-saving treatment should notify the HSRO of this intent by any available means (NOTE – a Pre-Emergency Use Notification Form is available on the HSRO website at http://HSRO.miami.edu). This notification must include:

a. a description of the circumstances that warrant the administration of a test article without IRB approval.

b. a statement that the subject is confronted with a life-threatening situation that requires immediate medical intervention before the IRB can be convened.

c. confirmation that no alternative method of approved or generally recognized therapy is available to provide an equal or greater likelihood of saving the subject's life.

d. a description of how the test article will be used.

ez. a copy of the informed consent document to be used; or

   i. A statement that the informed consent document cannot be obtained because of difficulty in communication with the subject and/or insufficient time to contact the subject's legal representative.

   ii. Both the primary physician and a physician who is not participating in the clinical administration of the test article must sign this document.

The HSRO shall forward the physician’s notification to the IRB chair or designee who will review the circumstances of the “emergency use” to verify whether it meets the conditions of 21 CFR 56.102 and he/she, or the HSRO, shall so notify the physician. This notification should not be construed as IRB approval. Rather, the HSRO shall use this prior report to initiate tracking to ensure that the investigator files a report within the five day time-frame required by 21 CFR 56.104(c).
Physicians authorizing the “emergency use” of the test article should follow as many subject protection procedures as possible including:
   a. obtaining an independent assessment by an uninvolved physician
   b. obtaining authorization from the IND/IDE holder (as appropriate)
   c. notifying institutional officials as specified by clinical/institutional policies
   d. obtaining informed consent from the patient or a legal representative
   e. notifying the HSRO

Within five (5) working days following the emergency use of a test article, the physician must notify the IRB in writing of the emergency use of a test article pursuant to FDA regulations at 21 CFR 56.104(c). This report should include an explanation of the use, how and when the use took place, and justification based on FDA criteria for “emergency use” including why prospective IRB review was not possible, the informed consent process, and, if applicable, how IND/IDE requirements were met. This report should include a copy of the properly executed (signed) informed consent document or a statement that informed consent document could not be obtained because of difficulty in communication with the patient and/or insufficient time to contact the patient’s legal representative. The report should also include follow-up information on the condition of the patient in the days after the test article has been administered. An “Emergency Use Report Form” is available on the HSRO website to ensure that all required issues are addressed. The form should be submitted with a copy of the consent form that was (or is about to be) signed by the subject or the subject’s authorized representative.

If further uses of a test article are anticipated, a study application must be submitted for review and approval by the convened IRB in addition to the submission of the 5-day report. Subsequent use of the test article is contingent upon this IRB approval and an FDA-approved IND/IDE.

There are two options available to applications for further uses of a test article.

   a. Not collecting data for research: If the test article use does not include collecting data for research purposes, a treatment IND/IDE should be obtained from the FDA and a corresponding study application should be submitted for IRB approval. IRB approval is required for the use of a treatment IND even if the use does not involve research.

   b. Collecting data for research: if research data is collected pursuant to the use of the test article, a research IND/IDE should be obtained from the FDA and a corresponding study application should be submitted for IRB approval.

**NOTE** - FDA acknowledges that it would be inappropriate to deny emergency use of an investigational drug or biologic considered necessary for the treatment of a second individual if the use was unexpected and the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue. Subsequent emergency use the unapproved article may not occur unless the physician or another person obtains approval of an IND/IDE. If the application for subsequent is disapproved by the FDA, the article may not be used even if the circumstances constituting an emergency exist. Manufacturers or developers of investigational articles that could be used in emergencies should anticipate the likelihood of emergency use and should obtain an IND/IDE for such uses.
FDA regulations do not permit expedited IRB approval in emergency situations and terms such as “interim,” “compassionate,” or “temporary,” may not be used to authorize an expedited approval process. IRB approval of an emergency use requires review by the convened panel or, if the conditions of 21 CFR 56.102(d) are met and it is not possible to convene a quorum within the time available, the emergency use may proceed without an IRB approval (providing all requirements are met).
27.4 EMERGENCY USE AND INFORMED CONSENT

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: August 24, 2008

Even for an emergency use, the investigator is required to obtain informed consent of the subject or the subject’s legally authorized representative, unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following [21 CFR 50.23(a)]:
1. The subject is confronted by a life-threatening situation necessitating the use of the test article.
2. Informed consent cannot be obtained because of an inability to communicate with or to obtain legally effective consent from the subject.
3. Time is not sufficient to obtain consent from the subject’s legal representative.
4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject’s life.

If an investigator believes immediate use of the test article is required to preserve the subject’s life and there is insufficient time to obtain an independent physician’s determination that the four conditions above apply, the clinical investigator may alone make the decision to use the test article. The investigator must then have his/her decision reviewed and an evaluation made in writing by a physician not participating in the clinical investigation. This review and evaluation must be made within 5 working days of the use of the test article. The investigator must also notify the IRB within 5 working days after the use of the test article [21 CFR 50.23(c)].

When non-therapeutic or therapeutic research that does not involve the use of a non-approved drug or device is considered in an emergency setting (not necessarily for the purpose of the emergency itself), proper consent procedures must be followed. Federal regulations offer some flexibility for such research; however, there are still appreciable requirements for which adherence is mandatory. In addition, Florida statutes (in particular the Medical Practice Act) are more restrictive for research in emergency settings than are federal regulations and may override the latter.

A template “Investigational Product Consent Form,” which may be amended to specific situations, is available on the HSRO website.
SECTION 28: RECORD RETENTION
28.1 General Principles

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: September 15, 2008

As defined within Section 24 of these policies, all records and documents relating to research studies and participants must be kept confidential to the extent permitted by law; however, records and documents shall be available in a timely manner to University authorized employees or other agents authorized by the University including IRB members and HSRO staff and appropriate governmental agencies including but not limited to the DHHS, OHRP and the FDA. All others requesting access to or copies of confidential study records and documents must obtain written approval from the Principal Investigator or the Associate Vice Provost for Human Subject Research. The Principal Investigator must describe in study documents for review by the IRB, and in consent forms, the extent, if any, to which confidentiality of study records identifying the subject will be maintained.

Although principal investigators are responsible for the creation and maintenance of research records and documents, such records and documents (including data collected pursuant to research) are the property of the University. Until the temporal requirements for record/document retention are met (c.f. Section 28.2- below), investigators or others may not remove or destroy research records or documents (or copies of such records or documents) without written permission from an authorized representative of the University. This permission requirement extends to investigators leaving the University even if they plan to continue the research at another institution.
28.2 RECORD/DOCUMENT RETENTION REQUIREMENTS

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: September 15, 2008

Study documents and/or records acquired by the IRB or principal investigators shall be retained according to the terms of federal regulations and Florida statues. Pursuant to federal regulations [c.f. 45 CFR 46.115(b) and 21 CFR 56.115(b)], the HSRO shall be responsible for maintaining its documentation, files and IRB meeting minutes relevant for each study for a minimum of three (3) years following IRB approval of the closure of the study.

With certain exceptions, Principal Investigators must retain complete records and documents (including the consent documents) from their study for the duration of that study and for a minimum period of three (3) years following closure of a study. Exceptions to this 3-year minimum retention period are:

a. HIPPA REQUIREMENTS: - if a study involves the collection of identifiable health information, principal investigators must retain study records and documents for six (6) years following study closure. This retention period is consistent with the HIPAA Privacy Rule under which subjects may ask investigators for an accounting of all uses and disclosures of their study information for a period of 6 years after their participation is completed (c.f. 45 CFR 164.528).

b. FDA REQUIREMENTS FOR A STUDY INVOLVING AN INVESTIGATIONAL DRUG UNDER AN IND (c.f. 21 CFR 312.62): if a study involves the use of an investigational drug under an IND, principal investigators must retain study records and documents until at least the later of the following dates:
   1. 2-years following the date a marketing application is approved for the drug for the indication for which it was being investigated; or,
   2. 2-years after the investigation is discontinued and the FDA is notified if no marketing application is to be filed or, if the application is not approved for such indication; or
   3. 3-years after IRB approval of the closure of the study
c. **FDA REQUIREMENTS FOR A STUDY INVOLVING AN INVESTIGATIONAL DEVICE UNDER AN IDE (c.f. 21 CFR 812.140):** if a study involves an investigational device under an IDE, principal investigators must retain study records and documents until at least the later of the following dates:

1. 2-years following the date on which the investigation is terminated or completed; or
2. 2-years following the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol; or
3. 3—years after IRB approval of the closure of the study

**NOTE** – The FDA two-year requirements may occur during the applicable retention period required by the University and other regulations or it may occur afterward and be additional to that period.

d. **VA REQUIREMENTS:** if a study engages the VA, principal investigators must retain research records and documents for a minimum of five (5) years after IRB approval of study closure. This retention period is consistent with the VA’s Records Control Schedule (RCS 10-1).

Records must be retained longer than the times specified in the above policies other requirements apply such as may be forthcoming from sponsors in executed contracts, institutional entities or extramural funding agencies.
28.3 RECORD/DOCUMENT STORAGE AND DELETION

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: September 15, 2008

Plans for the maintenance and storage of study records and documents must be submitted by the principal investigator to the IRB for approval. These plans should define record storage procedures and conditions and identify those with access to the records. Electronic data should be saved on a device that has appropriate security safeguards to protect against data loss or theft and to avoid any potential breach in subjects’ privacy and confidentiality. IRB approval shall be based on documented assurance that all hard copy and electronic data is securely stored to prevent unauthorized access, disclosure, or loss. Principal Investigators should also submit for IRB approval provisions for destruction of study records after the required data retention period has elapsed if the destruction of study records is necessary for confidentiality or other matters that protect participants.
OTHER POLICIES
INVESTIGATIONAL DEVICES

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: February 8, 2005

If an investigational device does not have an Investigational Device Exemption (IDE) number, the IRB must categorize the device as either “significant risk” or “non-significant risk.”

A significant risk device is defined by 21 CFR 812.3(m) as a study device that presents potential for serious risk to the health, safety, or welfare of a subject and:

1) Is an implant; OR
2) Is used in supporting or sustaining human life; OR
3) Is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; OR
4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

A non-significant risk device is one that does not meet the definition for a significant risk study.

The risk determination should be based on the proposed use of a device in an investigation, and not on the device alone.

If the IRB decides the device is of “significant risk,” the investigator must be notified of the decision, the investigator must notify the sponsor to obtain an IDE number, or, if there is no sponsor, the investigator must contact the FDA to obtain an IDE number.
GENETICS RESEARCH

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: February 8, 2005

Genetics research may have significant implications with regard to a number of issues. Genetic characterization can affect employability and insurability and have a major psychological impact. For these reasons, genetic research must be undertaken with great sensitivity and awareness of its potential ramifications. The University has developed special consent forms that are required for genetic studies.
GENE THERAPY RESEARCH

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: February 8, 2005

There are additional requirements for this type of research. The Institutional BioSafety Committee of the University must first approve any gene therapy applications before they can be submitted to the IRB for approval. The proposed studies must fulfill all federal regulatory requirements before they can be undertaken. As with any protocol application, the IRB should request consultation from experts as necessary. For any approved gene transfer study, the IRB must perform continuing review at an interval not less frequently than once a year.
WOMEN AND MINORITIES IN RESEARCH

Review Responsibility: IRB Policy and Procedure Committee
Current Approval Date: February 8, 2005

As stated in its guidelines, the NIH Outreach Notebook of the Inclusion of Women and Minorities in Biomedical and Behavioral Research (1994), the NIH has concluded that the inclusion of women in research is sufficiently important that the only justifiable reason to exclude non-pregnant women of child-bearing potential from research is a compelling rationale that the proposed project would be inappropriate with respect to the health of the subject or the purpose of the research.

The policy statement referenced above pertains primarily to the inclusion of women as subjects in clinical trials. However, investigators should also aspire to the inclusion of women in behavioral and other forms of research unless there is a compelling rationale that the inclusion is inappropriate regarding the health of the subject or the purpose of the research.

In addition to requiring the equitable selection of women as research subjects, federal regulations require the equitable selection of minorities as research subjects [45 CFR 46. 111(a)(3)]. The equitable selection of minorities in research is important both to ensure that they receive an equal share of the benefits of research and to ensure that they do not bear a disproportionate burden of the risks.